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SURGERY FOR MITRAL STENOSIS

2017

Part 1

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THE purpose of this report is to summarize our experience to date with the surgical treatment of mitral stenosis. Thirty-two patients have been operated upon and have been followed for 2 to 20 months after operation. Two patients died during the immediate postoperative period and a third, three months after operation. The remaining 29 have survived, and all but 1 of 17 who have been observed for longer than six months have shown definite functional improvement.

Pathology

Functionally significant mitral stenosis is the pathologic end result of rheumatic mitral valvulitis and its subsequent healing. Its development requires many months. During the initial attack of rheumatic carditis, the clinical picture is dominated by the effects of myocardial damage, and mitral stenosis plays no role in altering circulatory dynamics. The first clinical manifestation of mitral valvulitis is the appearance of the apical systolic murmur of mitral insufficiency. In certain patients the auscultatory findings of "pure" mitral stenosis gradually evolve. In others, the features are those of uncomplicated mitral insufficiency, but the largest number present evidence of combined stenosis and insufficiency. With gradual healing of active myocardial lesions, the more stable pattern of chronic valvular disease becomes evident. These patients with fixed valve lesions are our primary concern.

Obstruction to blood flow across a narrowed mitral valve causes an elevation of pressure in the left auricle and the pulmonary veins, which is accompanied by a rise in pulmonary artery pressure. In many instances, the elevation of pulmonary artery pressure is simply the mechanical result of mitral valve disease. In other patients there is an associated, and often greater, obstruction to blood flow through the pulmonary arteriolar bed. Specimens taken for lung biopsy at the time of commissurotomy in the latter group of patents show medial hypertrophy and intimal sclerosis in the pulmonary arterioles. The physiologic objective of mitral commissurotomy is relief of pulmonary hypertension. The functional end result of surgical intervention will be determined

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NORMAL BICUSPID
VALVE
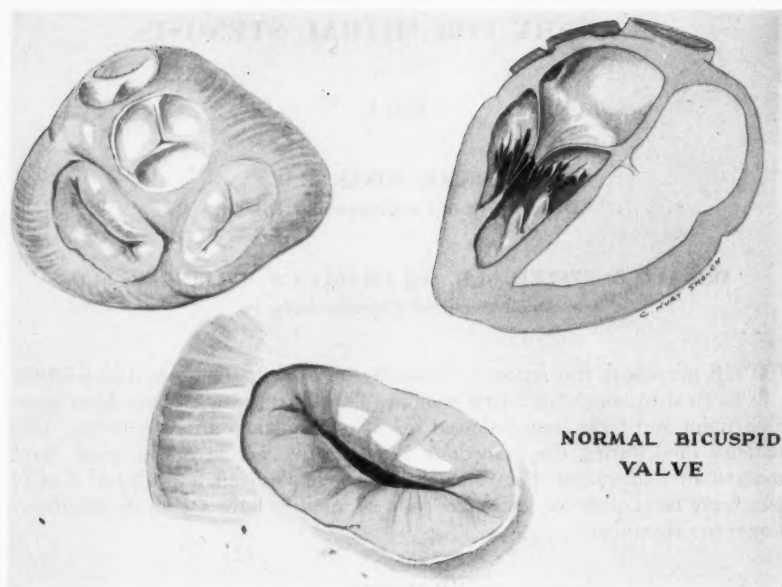
FIG. 1. Diagrammatic illustration showing topography and normal relations of mitral or bicuspid valve in the human heart.

by the degree to which these pulmonary vascular changes prove to be reversible, as well as by the increase in the size of the mitral valve orifice obtained.

Classification of Mitral Stenosis

On the basis of clinical and laboratory findings, patients with mitral stenosis may be divided into four functional groups.

Group I. Asymptomatic Patients. These are persons with the auscultatory findings of mitral stenosis who are able to carry on normal activities without symptoms. There is no significant cardiac enlargement. There are no specific electrocardiographic changes.

Group II. Patients with Symptoms Who Have Not Been in Congestive Failure. These are divided into two sub-groups.

(a) **Left auricular stress.** These people are comfortable in the absence of physical or psychic stress. Unusual physical or emotional strain causes marked dyspnea, and occasionally attacks of pulmonary edema. Left auricular enlargement is always present, but over-all heart size may be within normal limits.

(b) **Pulmonary hypertension.** Fatigue and dyspnea are present at ordinary levels of activity. Orthopnea in varying degrees of severity is experienced from time to time, and hemoptysis is not uncommon. The heart size is increased

because of left auricular and right ventricular enlargement. Electrocardiographic evidence of right bundle branch block or right ventricular hypertrophy is usually present.

Group III. Patients in Congestive Failure. These show the signs and symptoms of the Group II patients and also present systemic congestive manifestations which can be controlled by proper treatment.

Group IV. Patients with Intractable Congestive Heart Failure. The manifestations of congestive failure persist in spite of all measures of therapy.

Selection of Patients

Patients are selected for operation primarily on the basis of clinical evaluation of the disease. Cardiac catheterization has been routinely employed preoperatively. This has made possible objective measurement of the severity of abnormal resistance to blood flow through the pulmonary arteriolar bed and across the mitral valve orifice. It has been of value in dissociating subjective manifestations which are due to psychic factors from those due to organic disease. Similar studies made during the 3 to 12 postoperative months will be reported later.

VALVE IN ACTIVE
RHEUMATIC HEART
DISEASE
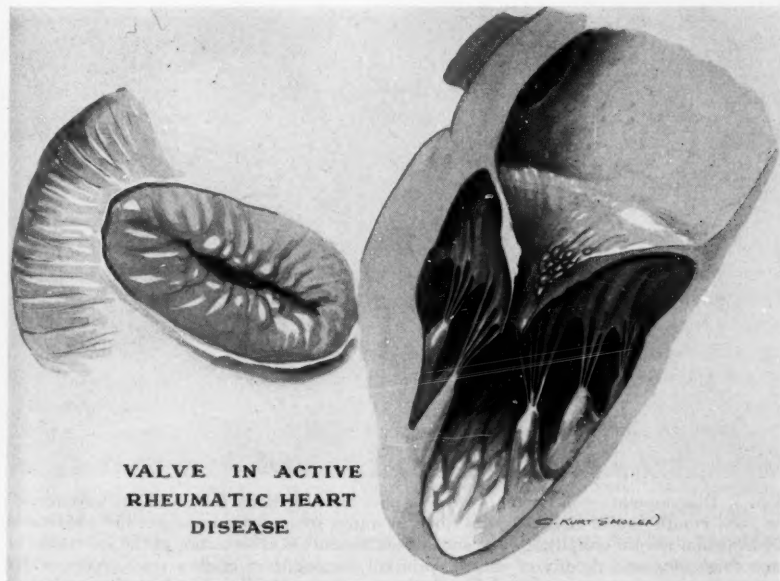
FIG. 2. Diagrammatic concept of mitral valve in active rheumatic heart disease. Valve edges become thickened by verrucous lesions associated with endocarditis. During this phase of the disease valve remains mechanically competent although the patient may be seriously ill.

At the present time operation is not advised in Group I patients. There is as yet no evidence that the prognoses of patients in this group are improved by commissurotomy. In Group IV patients, surgery is not recommended. The irreversible myocardial damage and secondary pulmonary vascular changes in this group cannot be significantly improved by surgical alteration of the mitral valve. Unless specific contraindications exist, all patients in Groups II and III are considered to be candidates for operation. The ideal candidates for operation are those in Group II.

Contraindications

Contraindications to mitral commissurotomy which seem to have been well established are listed below in the order of importance. Further experience may eliminate some of these and add others.

(1) Intractable congestive heart failure.

(2) Active rheumatic carditis.
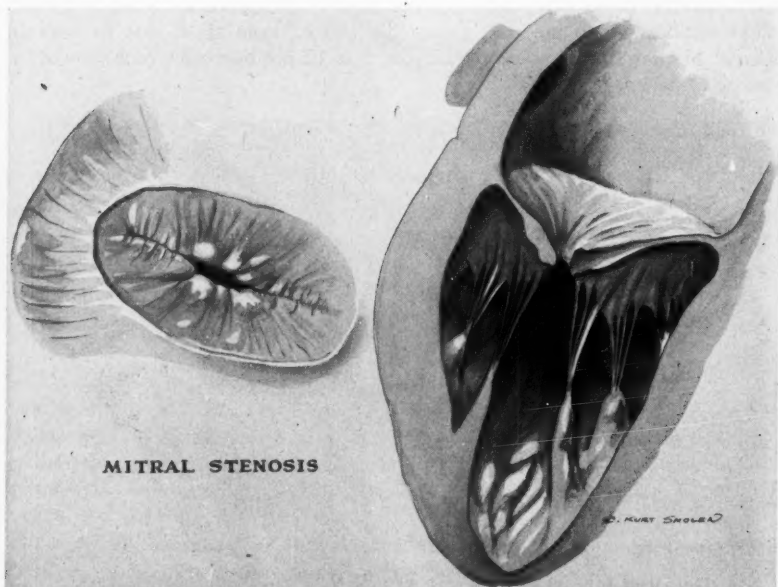
MITRAL STENOSIS

FIG. 3. Diagrammatic conception of valve in pure mitral stenosis, the so-called "buttonhole" or "fish mouth" valve classically described in mitral stenosis. Commissures are obliterated by avascular fibrous symphysis with central fixed lumen. On cross section of the valve observe that thickening and rigidity of valve is primarily in region of outflow tract. Where valve inserts on the ventricular and atrial wall there appears to be little residual disease. In this portion valve may be unusually thin and flexible.

NOTE: The artist did not attempt to depict the shortening and thickening of the chorda tendineae which usually accompany mitral stenosis.

(3) Functionally significant aortic valve disease or mitral insufficiency.

(4) Active bacterial endocarditis or systemic infections.

(5) Recent (within six to eight weeks) systemic or pulmonary embolism.

(6) Coronary heart disease with angina pectoris or previous myocardial infarction.

(7) Co-existing disease which limits a reasonable estimate of life expectancy to less than five years.

Selection of the proper time for operation may be a difficult problem. It is believed that a period of two years should elapse after the last episode of rheumatic activity. Since the primary concern is the ultimate fate of the valve after surgery, any factor which favors further deformity should be eliminated. Active inflammation of the valve at the time of surgery may stimulate re-approximation of the cusps, whereas this is not anticipated in the avascular, fibrous stenosis of old rheumatic heart disease. In addition to the evaluation of rheumatic activity the factors of recent congestive failure and embolic accidents influence the timing of commissurotomy. Operation is an elective procedure and is never regarded as an emergency measure. Thorough control of all congestive manifestations, eradication of infection, and the maintenance of a stable cardiac rhythm are essential in preoperative preparation. The presence of auricular fibrillation, if the ventricular rate is controlled at resting rates of 70 to 80 beats per minute, does not add to the hazard of surgery. Digitalis is used to control the ventricular rate in the presence of auricular fibrillation and in the presence of congestive heart failure. It is not indicated preoperatively in Class II patients who have normal cardiac rhythm. The use of atropine before induction of anesthesia is contraindicated.

Anesthesia

Safe anesthesia for surgery in mitral stenosis requires a technic which will give the most analgesia and amnesia for the least amount of anesthetic agent. The method employed at present utilizes endotracheal gas and oxygen under positive pressure. This is supplemented by local procaine (1 per cent) in the chest wall and intravenous procaine (2 per cent) given intermittently throughout the operation. Intravenous procaine has a double effect; it assists in control of cardiac arrhythmias by reducing the myocardial irritability, and it seems to enhance the effectiveness of the inhalation agents during light anesthesia.

The importance of positive pressure anesthesia deserves emphasis. Oxygen is the key to safe cardiac surgery. Positive pressure oxygen must be maintained in high levels of concentration from the period of induction throughout the operation, and until reaction has been complete. The lungs are kept expanded at all times even though this may make forcible retraction necessary during the operative procedure.

Pentothal sodium is employed only in the induction. The induction is performed in the patient's room and not in the operating pavillion. Apprehen-

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sion in the patient with mitral stenosis will result in tachycardia and a consequent increase in pulmonary hypertension. When intubation has been effected and the patient is converted to the inhalation agents, little or no pentothal is required. With experience there has been a tendency to omit ether. In the presence of severe pulmonary hypertension and its secondary changes in the tracheobronchial tree, ether is a tracheobronchial irritant, and greatly increases the postoperative pulmonary secretions. The patient with mitral stenosis may be carried on an unbelievably light plane of inhalation anesthesia without jeopardizing the surgeon's exposure. The majority of patients will respond to auditory stimuli during all phases of the operation, including the time of the actual commissurotomy. The patients are usually wide awake at the time they are removed from the operating table to the recovery room.
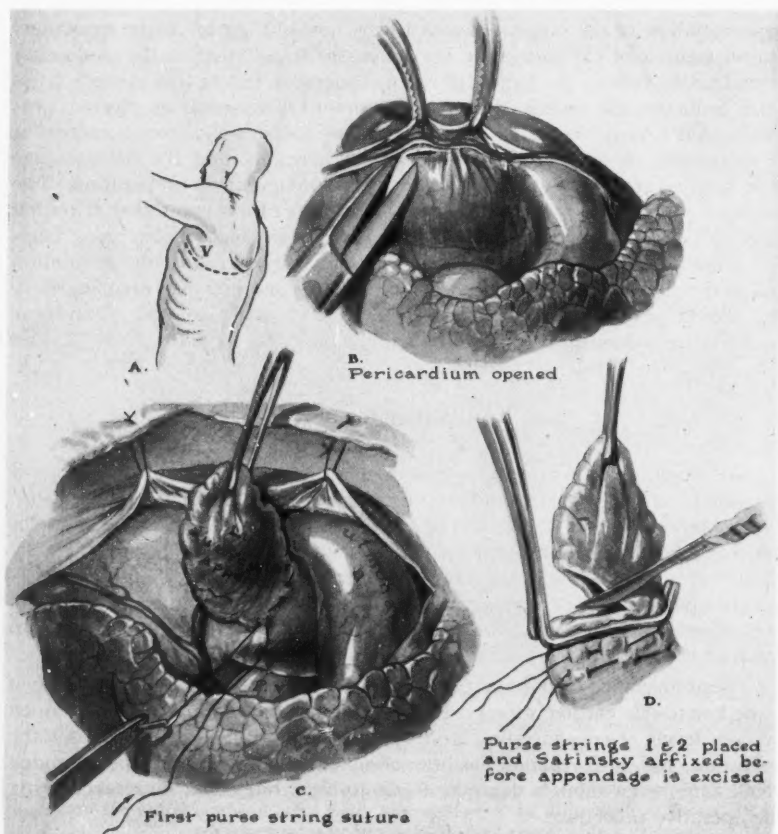
Fig. 4. Technic of operation is illustrated by diagram. (A), (B), (C), and (D) illustrate steps employed in performing auricular appendectomy.
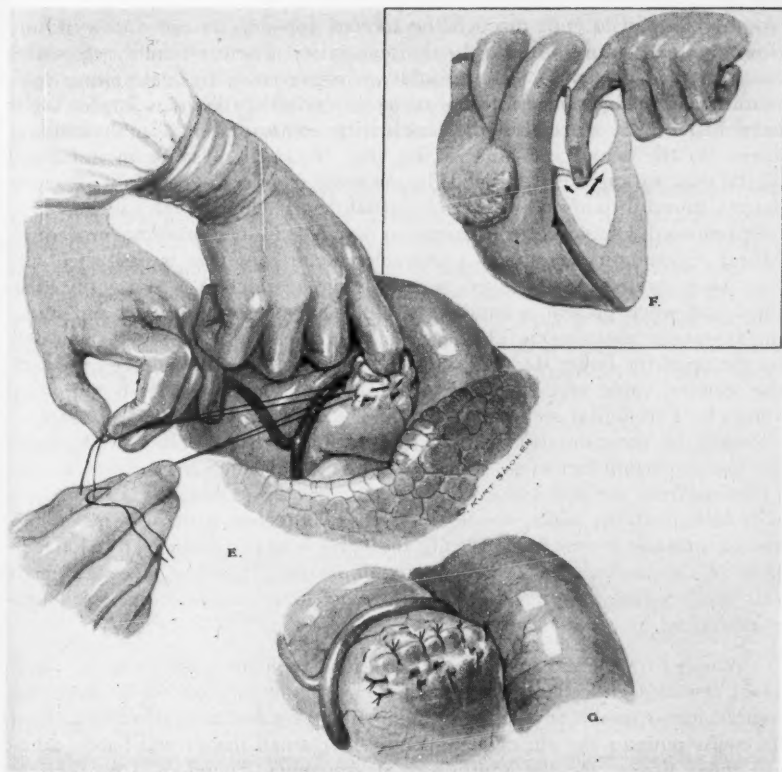
FIG. 5. (E) "Digital visualization" of diseased valve is accomplished with the aid of hemo-static purse string sutures around base of auricular appendage. (F) Cross section illustration showing range of examination by index finger. Arrows indicate lines of the two commissures of diseased mitral valve. (G) Obliterated auricular appendage following completion of procedure.

Operation

A modified posterolateral approach is employed, usually removing the fifth rib or going through the fifth interspace (fig. 4A). The expanded lung is retracted by the assistant and the pericardium is incised generously, usually on a line posterior to the phrenic bundle, carefully avoiding injury to the phrenic nerve (fig. 4B). The auricular appendage is examined and two purse string sutures are placed around its base; the second is a precaution in the event of accidental breakage of the hemostatic suture (fig. 4C). A non-crushing angle-clamp is placed across the base of the appendage and the tip of the appendix amputated (fig. 4D). The appendage is then carefully inspected for the presence of thrombi. If thrombi are present the clamp is removed and

blood is allowed to gush through the severed appendix in order to wash any fresh mural thrombus out into the thoracic cavity. The cavity of the appendix is repeatedly lavaged with saline solution to prevent a fresh thrombus from forming and being pushed into the auricular cavity by the index finger. As the index finger is introduced into the auricle with release of the clamp, the assistant draws up the hemostatic purse string (fig. 5E). This permits an unhurried digital exploration of the auricle. The auricular chamber is palpated for septal defects, mural thrombi, and other abnormalities. The mitral valve is then carefully palpated. Considerable information may be obtained from this procedure. Mitral regurgitation produces a characteristic stream that is easily felt and may be evaluated quantitatively to some degree. Calcium is also easily identified and when present is handled carefully to prevent fracturing and subsequent embolic phenomena. The degree of stenosis can be determined accurately by the tip of the finger (fig. 5F). Usually the finger tip will completely occlude the stenotic valve and effectively interrupt the blood flow from auricle to ventricle. This digital occlusion is used later to determine the degree of patency obtained by the commissurotomy. The thickness and pliability of the valve are also important factors in estimating the extent of the disease process and the prognosis from the standpoint of operative correction. Obviously a thick valve with little pliability will never be an effective competent structure even though the commissure is reopened. Ideally the valve is opened bilaterally along the lines of the medial and the lateral commissures. However, when extensive calcification has obliterated one of these two landmarks a unilateral commissurotomy is usually sufficient.

Whether the commissurotomy is performed by finger fracture or by instrument depends entirely upon the judgment of the surgeon. With increasing experience we tend to favor finger fracture as a safer and more effective method. In many patients the auricular appendix is so small that it will barely admit the index finger, and the addition of an instrument therefore is not feasible. Also variations in the topography of individual hearts make accurate incision by "manual vision" subject to a certain range of error. Finger fracture has proved reliable and adequate in the majority of patients. At the completion of commissurotomy the valve is palpated to detect any regurgitant stream incidental to the procedure and to evaluate the outflow tract of the "restored" mitral valve. Usually the operation is concluded without producing regurgitation or increasing that which was already present. Ideally commissurotomy permits free motion of the valve leaflets with an increase in effective valve area of approximately 200 to 400 per cent. Whereas the tip of the index finger would occlude the stenosed lumen prior to operation, the valve will usually admit two fingers or more after commissurotomy is completed.

When the finger is withdrawn from the heart, the purse strings are brought up tightly and the stump of the auricular appendage is closed with vertical mattress silk sutures (fig. 5G). The pericardial incision is closed loosely to allow free drainage into the left pleural space. A biopsy is taken of the lung for histopathologic studies, and the chest is closed with closed catheter drainage.

The entire operation is carried out with continuous electrocardiographic monitoring. The importance of cooperation between the anesthetist, cardiologist, and surgeon cannot be overemphasized. Many of the arrhythmias that might seriously complicate the operative procedure are anticipated and avoided by continual observation of the electrocardiographic record. There have been no uncontrolled arrhythmias.

Postoperative Management: The average period of hospitalization postoperatively has been 14 days. Most patients are able to sit up and feed themselves by the third postoperative day, and are allowed bathroom privileges on the seventh to tenth days. At the time of discharge, a bed and chair regimen at home is advised for the first two weeks. The patient is then allowed to gradually increase physical activity, being careful to remain within his exercise tolerance. Fatigue and dyspnea are avoided under all circumstances. Maximal activity tolerance is usually attained by the third or fourth month after operation.
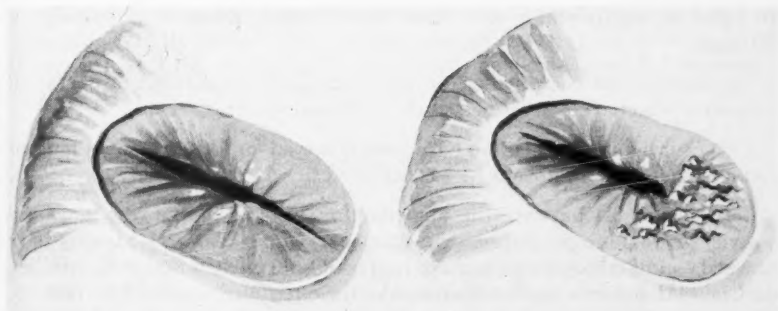
FIG. 6. A comparison with the diseased valves sketched in Fig. 3 will emphasize the increase in lumen produced by commissurotomy. Valve depicted on the left has bilateral commissurotomy and represents the ideal surgical result. Valve depicted on the right illustrates a common finding when one commissure is replaced with superimposed calcareous deposits. Actually this calcium may resemble stalagmites. An attempt to fracture or cut through this portion of valve will increase the hazard of embolism by fragments of calcium. A generous incision in the opposite commissure will frequently suffice for a good clinical result.

A low sodium diet is advised for all postoperative patients during the first six to eight weeks. This is not necessary thereafter in Class II patients. Class III patients require salt restriction for longer periods of time, and in some instances this may be a permanent measure.

Occasionally during the first three months after operation there are recurring episodes of left anterior and lateral chest pain which may be quite distressing. These are not accompanied by evidence of pericarditis or pleuritis. The pain is usually aggravated by motion of the shoulder girdle but may be continuous. It is relieved by salicylates and codeine when necessary and disappears in one to four days. This problem has not been encountered after the fourth postoperative month.

All patients with sinus rhythm are given Pronestyl during the first three months after operation. It is then discontinued. No patient treated in this manner has developed auricular fibrillation after operation, although this was a frequent complication before Pronestyl was used.

Results

Ten men and 22 women, aged 21 to 54 years, have been observed for from 2 to 20 months after operation. Two patients belonged to Class II(a); 11 were in Class II (b); 18 were in Class III, and one in Class IV.

Two patients died shortly after operation, one of cerebral embolism which occurred during operation, and one of hemorrhage and cardiac tamponade. The third patient who died after operation was the only Group IV patient in the series. This man had severe mitral insufficiency as well as mitral stenosis. He failed to improve and died three months after operation of pulmonary embolism.

No attempt has been made to evaluate the functional result of operation in patients who have not yet passed the sixth postoperative month.

Of 17 surviving patients who have been observed for longer than six months obvious functional improvement has occurred in 16.

Of 11 Class III patients, the single failure occurred in one who had been in congestive failure for longer than four years. Four Class III patients have returned to full employment and are supporting themselves and their families. Six Class III patients are housewives who have resumed normal activities.

All five patients in Group II (b) have shown satisfactory improvement. Despite increased levels of activity none has suffered hemoptysis or pulmonary edema. There has been no recurrence of nocturnal dyspnea or orthopnea.

The remaining patient in Group II (a) is now regularly employed as a truck driver. He is entirely asymptomatic.

There have been no embolic complications in any of the surviving patients.

Summary

Preliminary clinical results in 32 patients with mitral stenosis, treated by mitral commissurotomy, are summarized.

Clinical criteria used in the selection of patients for operation and the contraindications to surgery are discussed.

The essential factors in pre- and postoperative management and the technic of operation are briefly described.

POPLITEAL ANEURYSM

Treatment by Vein Graft: Case Report

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THE popliteal artery is the second most common site of aneurysm. The treatment of this condition has been reviewed frequently and various methods have been suggested to restore normal anatomy.[1-13]

A patient was recently seen suffering from bilateral popliteal aneurysm. One side was treated by resection and sympathectomy; the other by venous homograft technic. An unusual opportunity has been provided to compare the results of the two procedures in the same patient.

Case Report

The patient, a 59 year old man, was admitted to the Clinic complaining of recurrent attacks of pain in both lower extremities. A review of the history indicated that for two years prior to admission he had been aware of slight leg fatigue following exercise. At no time did he have intermittent claudication. Eight months prior to admission, he experienced a sudden attack of severe knife-like pain in the left calf which occurred while walking. No unusual coldness, numbness, or color change was noted. The attack of severe pain lasted two days and gradually subsided. Three months following this attack, he had a second severe episode of pain in the left calf, lasting several days. One week before admission to the Clinic, he developed a similar attack of pain in the right calf. Following each attack petechiae were observed over the involved extremity. No pain was noted between attacks but leg fatigue continued to occur following exercise. At no time was there evidence of swelling. Local tenderness to pressure was noted at the time of all attacks.

Examination of the lower extremities revealed the feet to be warm and of normal color. A few superficial varicosities were noted. The dorsalis pedis and posterior tibial pulses were of good quality. Examination of the left popliteal fossa revealed a pulsating mass approximately 8 cm. by 4 cm. in size. Examination of the right popliteal fossa disclosed a slightly smaller pulsating mass. The retinal vessels demonstrated no significant changes. No evidence of cardiac enlargement was found and the heart sounds were normal. The blood pressure was 210/130. Laboratory studies including roentgenographic examination of the chest, electrocardiogram, and renal function tests were normal. Our clinical impression was (1) essential hypertension, and (2) bilateral popliteal aneurysms with secondary arterial emboli involving the calf region. Hospitalization was advised and the following procedure carried out.

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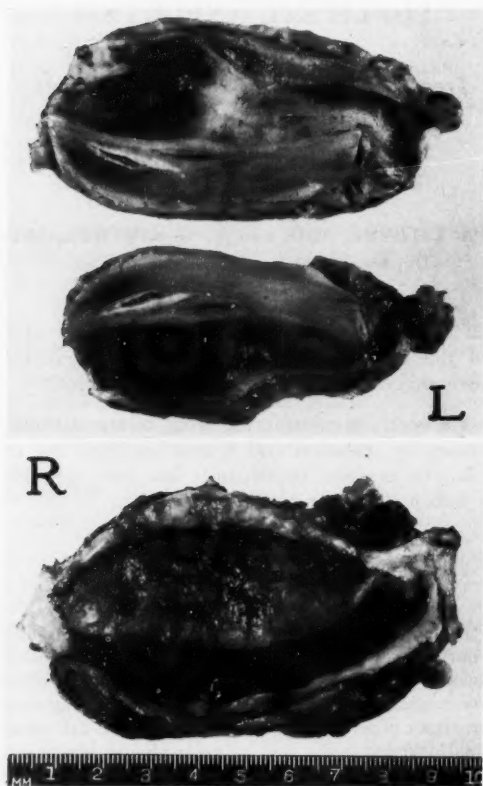
FIG. 4.

The aneurysm on the left side was exposed and found to be 11 by 4 by 5 cm. (fig. 4). The wall of the aneurysm was sclerotic with areas of yellowish degeneration which were soft and it was felt inadvisable to attempt direct repair. The cut ends of the artery were ligated and no major collaterals were sacrificed. A left lumbar sympathectomy (L1-L3) was done immediately following the foregoing procedure. Nine days later, the right popliteal aneurysm was completely excised and found to be 10 by 5 by 5 cm. (fig. 4). A vein graft was introduced to establish continuity of the vessel (fig. 1). The lesser saphenous vein was transected distal from its entrance into the popliteal vein. The end of the vein was swung up and anastomosed to the proximal cut end of the popliteal artery, thus permitting a flow of blood through this artificial arteriovenous fistula. The distal end of the popliteal artery was then prepared for anastomosis. The use of this technic (Julian[15]) insures reversal of the vein direction, thus eliminating the problem of the vein valves. The lesser saphenous vein was again transected prior to its entrance into the popliteal vein to give a vein segment slightly shorter than the missing portion

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of the popliteal artery. The vein was swung down, and anastomosed to the distal end of the artery. Following this, an emphatic pulsation was noted in the grafted vein and a strong pulsation in both the dorsalis pedis and posterior tibial artery. This area was drained for two days and the postoperative course was uneventful. No anticoagulants were used.

Bed rest was continued for six days and then light activity was permitted. The postoperative right femoral arteriogram is shown in figure 2 and the left in figure 3. The clinical course to date has been satisfactory. The right leg feels normal to the patient. The foot has remained warm and of normal color with good dorsalis pedis and posterior tibial pulsations. Slight edema, noted after prolonged standing, has been controlled with an elastic support. Some distress involving the left side has been experienced. This consists of numbness of the foot, and pain in the distribution of the ilio-inguinal and iliohypogastric nerves. The foot pulses are, of course, absent. The foot is warm and of good color. No intermittent claudication has been noted.
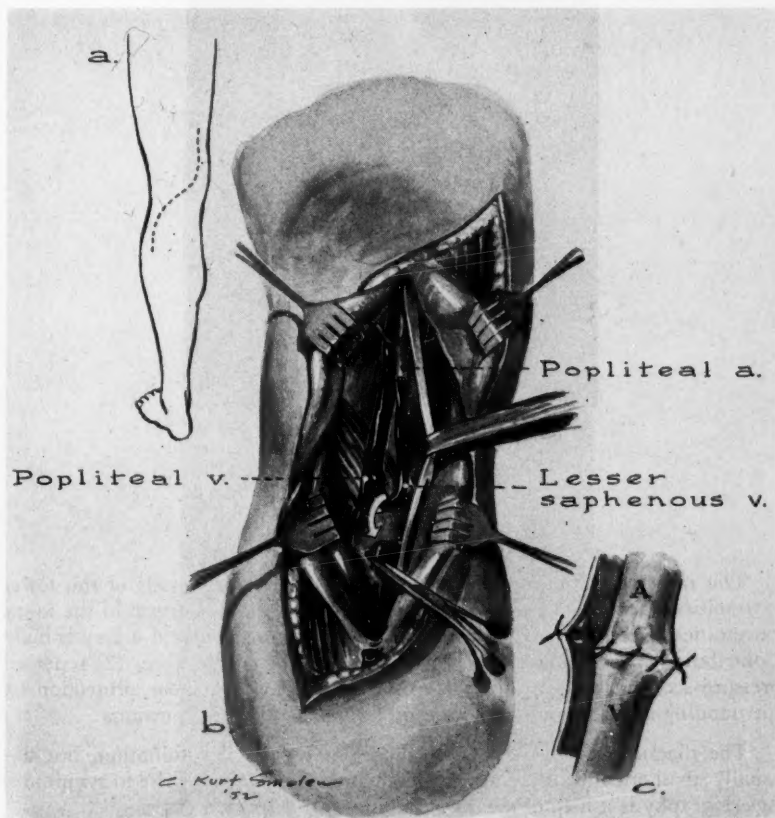
FIG. 1. (a) Incision. (b) Exposure and first anastomosis. (c) Technic of anastomosis.

FIG. 2.

Comment

The most common cause of aneurysms of the large vessels of the lower extremities is arteriosclerosis. Syphilis is a rare cause of aneurysm in the lower extremities. The incidence of aneurysm involving the popliteal artery is high. Contributory factors may be: (1) frequent bending of the knee, (2) repeated pressure secondary to sitting and crossing the knees, (3) poor protection by surrounding muscles, and (4) a location frequently subject to trauma.

The diagnosis can generally be made on physical examination, but unusually small aneurysms are not palpable and these may give rise to symptoms. Arteriography is a helpful means of diagnosis in suspected cases.

In all cases excision of the aneurysm is beneficial, not only for elimination

of the disease but for the following reasons: (1) it removes a space-consuming lesion which may compress the collateral circulation; (2) full flexion of the knee may be restricted in the presence of aneurysm; (3) the size of the aneurysm may cause stretching of the artery in the region of the collateral ostea thus reducing the collateral circulation.

In 1947 Blakemore[14] presented a technic of vein graft inlay for the repair of arterial aneurysm using vitallium tubes. Four cases were reported, one a popliteal aneurysm.

The use of venous grafts as suggested by Julian et al.[15] in the treatment of segmental arteriosclerosis obliterans of the lower extremities offers a means of reestablishing the circulation. We believe this method can be applied to the popliteal artery for the treatment of aneurysm.

FIG. 3.

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Summary

A case of bilateral popliteal aneurysm has been presented.
A venous homograft was successfully employed on one side.

References

1. Hufnagel, C. J.: Popliteal aneurysm: 2 cases. M. Bull. Vet. Admin. **20**:86-90 (July) 1943.

2. Theis, F. V.: Popliteal aneurysms as cause of peripheral circulatory disease: with special study of oscillomographs as aid to diagnosis. Surgery **2**:327-342 (Sept.) 1937.

3. Theis, F. V.: Peripheral arterial aneurysm: diagnosis, prognosis, and treatment. Internat. Clin. **2**:205-216 (June) 1940.

4. Keynes, G. L. and Morel, M. P.: Popliteal aneurysm. Brit. J. Surg. **31**:155-157 (Oct.) 1943.

5. Blakemore, A. H.: Amputation for aneurysms. S. Clin. North America **18**:409-414 (April) 1938.

6. Wells, A. H., Coburn, C. E. and Walker, M. A.: Popliteal aneurysm, with report of case. J.A.M.A. **106**:1264-1266 (April 11) 1936.

7. Flemming, C.: Aneurysm of both popliteal arteries. Lancet **1**:322-323 (Feb. 11) 1939.

8. Matas, R.: Endo-aneurysmorrhaphy. Surg., Gynec. & Obst. **30**:456 (May) 1920.

9. Bird, C. E.: Sympathectomy as preliminary to obliteration of popliteal aneurysms. Surg., Gynec. & Obst. **60**:926-929 (May) 1935.

10. Gage, M.: The development of the collateral circulation in peripheral arterial aneurysms by sympathetic block. Surgery **7**:792-795, 1940.

11. Richards, R. L. and Learmonth, J. R.: Lumbar sympathectomy in treatment of popliteal aneurysm. Lancet **1**:383-384 (March 28) 1942.

12. Linton, R. R.: Arteriosclerotic popliteal aneurysm; 14 patients treated by preliminary lumbar sympathetic ganglionectomy and aneurysmectomy. Surgery **26**:41-58 (July) 1949.

13. Lilly, G. D.: Management of aneurysms of lower extremities. Ann. Surg. **123**:601-609 (April) 1946.

14. Blakemore, A. H.: Restorative endo-aneurysmorrhaphy by vein graft inlay. Ann. Surg. **126**:841-849 (Dec.) 1947.

15. Julian, O. C., et al.: Direct surgery of arteriosclerosis. Ann. Surg. **136**:459 (Sept.) 1952.

OBSERVATIONS REGARDING THE PROGNOSIS AND DIAGNOSIS OF HYPERPARATHYROIDISM*

JOHN HELLSTROM, M.D.**

THE material consists of 31 cases observed during the period 1930 to 1952. Of these, 28 were operated upon; one was subjected to roentgen therapy only, and two received no treatment. Eighty-five per cent of the patients were women. Renal calcifications or concrements without visible bone changes occurred in 45 per cent. With or without concomitant skeletal changes renal calcifications appeared in 74 per cent. A single ureter stone can be the first symptom in hyperparathyroidism. Of great importance is the fact that hyperparathyroidism may be present, although there are other factors to explain the development of calculi. Thus among 31 patients, three were treated many years for chronic staphylococcuria with stone formation and underwent several operations before the hyperparathyroidism was diagnosed.

Less often appreciated than renal calcification, but probably of greater significance from the prognostic viewpoint, are the renal changes, which, though not detectable radiologically, appear in all cases of hyperparathyroidism and lead to a more or less severe reduction in renal function. The kidney damage chiefly manifests itself in a reduced concentrating power, while in the beginning the nonprotein nitrogen may be normal, the clearance good, and the urine albumin-free. Table 1 shows the mean values for nonprotein nitrogen, the clearance and the water test in the cases I observed.

Table 1

MEAN VALUES FOR NONPROTEIN NITROGEN,
CLEARANCE AND THE WATER TEST

N. P. N.	Clearance	Specific Gravity in Water Test
38 mg. per cent	82 ml./min.	1.006 to 1.012

In assessing the prognosis, the renal changes play a much greater part than the altered bone structure. Even a severe generalized osteitis fibrosa cystica can disappear functionally after a parathyroidectomy. Although the hyperparathyroidism disappears, kidney damage often persists and the patient dies from uremia.

Another interesting, and very important complication in hyperparathyroidism is a steadily rising blood pressure. Hypertension regularly occurs in most cases of hyperparathyroidism. This blood pressure elevation, though initially slight and often transitory, becomes more extreme and persistent with time. Eventually hypertension or one of its complications results in the patient's death. Considering the obscure pathogenesis of hypertension, it is not surprising that the blood pressure rise accompanying hyperparathyroidism should be hard to explain. It scarcely seems likely that the tubular pathologic condition produces hypertension. They are more probably conditions which run parallel to each other. As the disease progresses, the kidneys begin to play a progressively greater role in the aggravation of hypertension due to nephrosclerotic and pyelonephrotic changes. It is clear that patients who have had overactive parathyroids removed require constant observation; their hypertension will need appropriate treatment, perhaps eventually including surgery.

Table 2

LATE RESULTS AFTER REMOVAL OF SOLITARY ADENOMA

Case No.	Blood calcium	Renal damage	Hyper-tension	Cap. for work; gen. condition	Observ-ance time	Remarks
1	Normal	Increased	+	Excellent 13 years	20 years	Amput. both legs
3	Normal	Increased	+	Excellent 10 years	13 years	Died cerebral hemorrhage
4	Normal	Increased	+	Improved	7 years	Died nephro-sclerosis
8	Normal	Increased	+	Improved	8 years	Died uremia
9	Normal	Increased	+	Improved	8 years	Died nephro-sclerosis
10	Normal	Improved	+	Excellent	6 years	B. P. 200/100
11	Normal	Increased	+	Improved	7 years	Symptoms of hypertension
12	Normal	Improved	−	Excellent	6 years	Nephrolithiasis
13	Normal	Improved	−	Excellent	4 years	Nephrolithiasis
14	Normal	Improved	−	Excellent	2 years	Nephrolithiasis

Table 3

LATE RESULTS AFTER PARATHYROIDECTOMY IN CASES
WITH DIFFUSE HYPERPLASIA

Case No.	Blood calcium	Renal damage	Hyper-tension	Cap. for work; gen. condition	Observ-ance time	Remarks
2	Elevated	Increased	+	Improved several years	12 years	Died of uremia
5		Increased	+	Improved several years	10 years	Hypertension; invalid
6		No increase	+	Improved	11 years	Working as nurse
7		Increased	+	Improved	10 years	Severe hypertension

The prognosis in hyperparathyroidism, even after parathyroidectomy, has been somewhat ignored because of incomplete follow-up investigations. In cases of hyperparathyroidism due to an adenomatous change of only one of the parathyroid glands, removal of this adenoma regularly results in an immediate and usually permanent disappearance of the hyperparathyroidism. But kidney damage and hypertension often persist and progress. Also, after years of relatively good health many patients become permanent invalids and finally succumb to renal insufficiency or cerebral hemorrhage. This is clearly illustrated in table 2 which shows the late results after removal of an adenoma. It is to be expected that the late results should be less satisfactory in cases with so-called diffuse hyperplasia of all the parathyroid tissue. Surprisingly, some of these patients may live for a long time in a relatively good condition despite an incomplete operation and persistent hyperparathyroidism (table 3).

The prognosis of a patient with hyperparathyroidism is often definite at the time when the diagnosis is established. An early diagnosis is therefore most important.

In most cases a distinctly elevated calcium level is highly indicative of hyperparathyroidism. And yet hyperparathyroidism may be accompanied by normal blood calcium levels, as occur in patients with far advanced renal damage with retention of phosphates in the blood.

Of greater interest is a normal blood calcium level in early cases of hyperthyroidism. It can well be asked whether a determination of the different plasma calcium fractions would not be desirable, if a deranged calcium metabolism is to be unmasked.

In table 4 three of the cases are tabulated in which no change in the total serum calcium could be found; but the diffusible fractions' concentration exceeded the upper limit of what is considered normal. Remarkable, too, is the return of the diffusible fractions to normal following operation.

Table 4

PRE- AND POSTOPERATIVE
FRACTIONAL BLOOD CALCIUM DETERMINATIONS

Case No.	Preoperative		Postoperative	
	Total serum calcium	Free serum calcium	Total serum calcium	Free serum calcium
25	10.1	6.3	8.9	5.2
26	10.0	6.8	10.0	5.1
27	9.9	6.8	9.5	5.4

Conclusions

The best known and most striking findings typical of hyperparathyroidism are, on the one hand, the decalcification of the skeleton, usually in the form of generalized osteitis fibrosa cystica; and on the other, renal concrement or calculus formation. However, more important than these findings from the prognostic viewpoint are: (1) renal damage most probably involving the tubules particularly, and reflected chiefly in the decreasing concentrating power, and (2) a rise in blood pressure, usually progressive in nature. No direct connection between renal damage and hypertension has been found in the earlier stages of the illness when the blood pressure elevations vary greatly. With the arrival of the secondary nephrosclerotic and pyelonephritic renal changes, hypertension occurs which is more permanent and more definitely determined by the state of the kidneys.

The prognosis following hyperparathyroidectomy is essentially dependent on two factors: whatever renal damage may have already occurred; and, on the severity of the blood pressure rise occasioned by the hyperparathyroidism. Early diagnosis and surgery are therefore of vital importance. A full realization of the fact that the serum calcium may lie within normal limits in hyperparathyroidism should lead to the performance of repeated blood calcium determinations in cases where this condition is suspected.

Further investigations will show if a relative rise in the free, diffusible calcium fraction is sufficiently pathognomonic of hyperparathyroidism.

CONTINUOUS SPINAL ANESTHESIA IN COLON SURGERY

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PATIENTS requiring surgery of the large bowel are frequently poor operative risks because of age and degenerative vascular disease. The depleting effects of chronic or acute obstruction, large infected ulcerating cancers, and the ravages of ulcerative colitis also increase operative risk. Under such conditions impairment of the nutritional status and deficiencies in the circulating blood volume are found.

It has seemed wrong to us to subject such patients to the depressing and otherwise deleterious effects of anesthesia by ether and other inhalation agents. Single injection spinal anesthesia has the disadvantage of adding hypotension to the already depleted circulating volume. In the past three years we have used continuous spinal anesthesia administered in fractional doses. This type of anesthesia has several outstanding advantages. (1) The anesthetic can be confined to the area to be operated upon. (2) The total dose can be "controlled" and is minimal as compared to single injection technics. (3) Hypotension can be avoided or minimized by fractional doses. (4) Operative procedures of any magnitude may be carried out with little worry over time consumption since the anesthesia may be prolonged by added injections.

Since January 1950 we have used continuous spinal anesthesia to perform 505 resections of the colon with nine deaths; a hospital mortality of 1.7 per cent. There can be little doubt that the lowered mortality or morbidity in colon surgery is partially due to safer anesthetic methods.

Continuous spinal anesthesia administered in fractional doses with the ureteral type catheter causes minimal disturbance to the physiologic balance and gives adequate analgesia and relaxation. The level and extent of anesthesia which is necessary varies with the location and the character of the lesion. These levels range from a high of T3 for splenic and hepatic lesions to S5 for rectal lesions. If anesthesia by the classic spinal technic were to be induced between these extremes, many patients would react violently to the accompanying sympathetic nervous system paralysis. The splanchnic and the vasomotor nerves for the lower extremities originate within these levels. Complete vasodilatation of the vessels of the legs causes the circulating blood volume to be depleted by bleeding into the leg veins. Accompanying this relative diminution of the circulating blood volume, stasis results with the possible

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occurrence of venous thrombosis. By limiting the extent of anesthesia to a few dermatomes, these complications can be avoided. Saklad[1] has described a segmental type of spinal anesthesia produced by the ureteral catheter technic. A sensory level of anesthesia is obtained by properly placing the tip of the catheter so that analgesia is produced only within the operating zone. Frequently this involves only a few segments. Advantage may be taken of the anatomy of the spinal cord in reference to the innervation of the sympathetic nervous system. All efferent sympathetic nerves originate in the intermediolateral cell column of the spinal cord and travel over the anterior nerve roots to the sympathetic ganglia. Here the sympathetic nerves communicate by means of the sympathetic chain with other sympathetic nervous system neurons originating in the same manner two or three dermatomes above. Therefore, if the level of anesthesia would be limited to two or three segments, little or no vasomotor phenomena should be realized.

With the small fractional doses of anesthetic agent as administered in the segmental continuous spinal technic, anesthesia of the sensory and motor components of the spinal segments is complete. However, the sympathetic nerves can secure innervation from other levels. Pain and temperature anesthesia may extend into the neighboring dermatomes. The sensory and sympathetic nerves are affected first with blocking agents. With larger concentrations the motor fibers are blocked. Therefore, it may be postulated that due to the dilution of agent as it diffuses, there is little or no effect upon the sympathetic or motor components. As a result, segmental anesthesia with the ureteral catheter technic causes a sensory anesthesia of a calculated extent accompanied by adequate motor paralysis, but little or no sympathetic effect. The field of anesthesia is a restricted area of analgesia adequate for surgical manipulation but with muscle tone and vasomotor tone of the legs maintained to promote adequate circulation. This is important in the older age groups and may prevent formation of thrombus and subsequent pulmonary embolus. The disadvantage of the classical spinal anesthesia is thereby circumvented.

Method

Segmental spinal anesthesia is attained by using the ureteral type spinal catheter as introduced by Tuohy.[2] The tip is placed at a predetermined level. A 16 gauge Tuohy needle is inserted into the dural sac in a lower lumbar interspace at a 45 degree angle with the plane of the back (fig. 1a). With the needle in the subdural space, spinal fluid will flow freely. The catheter is then inserted into the needle as far as the Huber point. The level to which it is to be inserted is then measured with the catheter to the proper interspace (fig. 1b). It is then advanced with extreme care to the desired space. If paresthesia is elicited, the needle can be rotated through 45 degrees and the catheter inserted farther. A 2 cc. syringe is then fitted to the catheter with an adapter. With gentle suction, spinal fluid will be aspirated. The catheter is then securely taped in place and the patient is placed in the surgical position.
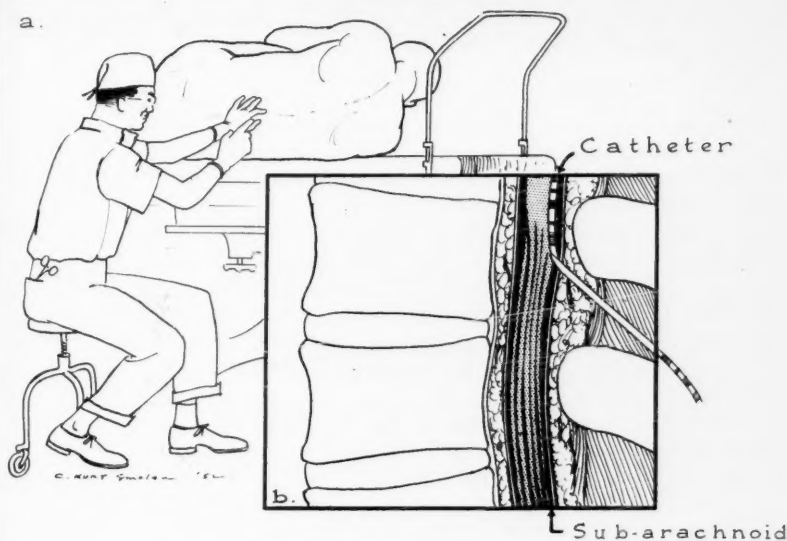
Fig. 1. (a) Position of the patient and the anesthesist for lumbar puncture. (b) Diagrammatic illustration showing placement of Huber point and the catheter lying in sub-arachnoid space.

To facilitate the administration of small doses and to prevent diffusion of effective quantities into other interspaces, a dilute solution of procaine 100 mg. and pontocaine hydrochloride 10 mg. in 10 cc. of normal saline is used. This mixture may be considered isobaric. The patient may be placed in any position without fear of diffusion throughout the spinal canal. Colon surgery frequently requires a Trendelenburg's position of 10 or 15 degrees. Administration of 1 or 2 cc. of this mixture will cause anesthesia at the determined level.

Fractional doses of the preceding mixture are administered in units of 1 cc. After the initial injection, five minutes are allowed to elapse. If no anesthesia is apparent, another unit is given. This is repeated until satisfactory anesthesia is obtained. Rarely is it necessary to administer more than three units for initial anesthesia. Subsequent or maintenance doses are administered when the patient becomes restless. Although pain sensation has not returned, muscle relaxation may soon disappear. One cubic centimeter of the procaine-pontocaine solution will give additional anesthesia for an average of 30 minutes. These subsequent doses are small and capable of prolonging anesthesia, the induction of which originally requires two to four times these amounts.

In the combined abdomino-perineal resection, it is often necessary to extend the level of anesthesia caudad. For the perineal phase in this instance, a hypobaric solution of niphanoid pontocaine (10 mg.) dissolved in water (5 cc.) is

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injected very slowly in doses of 1 cc. (fig. 2). With the patient in Trendelenburg's or Kraske's position, sensory anesthesia of the lower spinal roots will occur.

Most of the complications of ordinary spinal anesthesia are circumvented with segmental continuous spinal anesthesia. The initial injection of 1 cc. (10 mg. procaine and 1 mg. pontocaine) is seldom enough to cause hypotension. With five minutes elapsing before the second injection, time is available to evaluate the patient's condition. The blood pressure and pulse are recorded, the level and extent of anesthesia determined.

Frequently, the initial injection of one unit (10 mg. procaine and 1 mg. pontocaine) produces adequate conditions for surgery. If, however, the quality or extent of analgesia and relaxation are inadequate, and the circulatory signs unaffected, the second unit is injected slowly. In most instances, this quantity of agent presents ideal surgical conditions. Continuous and cautious evaluation of the patient is mandatory. Frequent pulse and blood pressure determinations are taken and recorded.

Fluctuations in blood pressure during the segmental type of continuous spinal anesthesia are minimal when compared to the single injection technic. In most instances, the initial and temporary fall of blood pressure is absent or
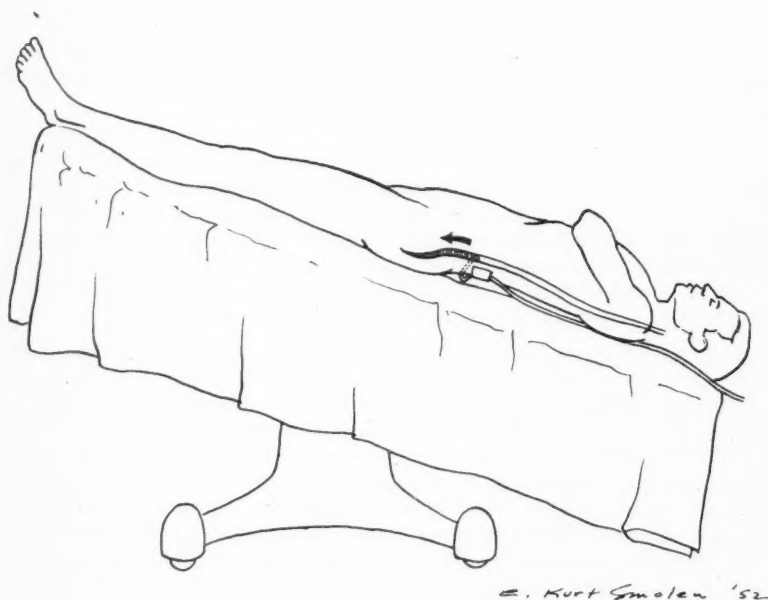
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FIG. 2. Drawing showing that portion of the spinal cord where anesthesia is produced by hypobaric solution. The arrow indicates the direction in which the anesthesia will occur

insignificant. Should hypotension of severe proportions develop, a vasoconstrictor such as neosynephrin (0.2 cc. or 1.0 per cent solution in 500 cc. of 5 per cent glucose in water) will readily correct the falling blood pressure. This solution is allowed to run rapidly by intravenous drip and can be regulated to maintain normotensive levels.

Supplementary agents are indicated only when the patient is nervous and apprehensive, or when traction discomfort becomes annoying. Routine sedation of the toxic and severely ill is avoided. When necessary for pain and discomfort, nembutal or seconal is administered intravenously in doses sufficient to sedate but not to produce unconsciousness. Nausea and vomiting are treated in the same manner. In addition, any hypotension must be corrected and oxygen administered via face mask. The total dose of pentothal sodium solution, if used in a prolonged case, becomes excessive. In the aged and toxic patient, the rapidity of onset and potent action may combine to adversely effect the delicate status of an already critically ill person. Other inhalation anesthetics are seldom used and certainly not advised.

Complications

Postoperative headache is the most common complication of continuous spinal anesthesia. In a previous series[4] the incidence was reported as 9 per cent. It must be explained, however, that the incidence of spinal headaches may not be accurately determined because the patient in many instances has been acutely ill and will not assume an erect position to precipitate the encephalalgia. Compared to other reports[5] this figure is favorable.

The possibility of neuropathies as a result of lumbar puncture and the catheter technic should not be overlooked. The plastic catheter when introduced through the 16 gauge Tuohy needle may touch or even irritate a nerve root. This increased danger is accepted so that the patient may have the benefit of an otherwise extremely safe and indicated anesthesia. Peripheral neuropathies occurred in two patients (an incidence of 0.4 per cent) both of whom are improved. Other postoperative complications, such as atelectasis, urinary retention, and phlebothrombosis, are only occasionally seen. There were no deaths resulting from anesthesia.

Summary

Since January 1950, 505 colon resections have been performed under continuous spinal anesthesia. There have been nine hospital deaths or 1.7 per cent mortality. The main complication following this type of anesthesia has been postoperative headache. No patient has been incapacitated in any way. Since the anesthesia is regional and nontoxic, and since hypotension is unusual, it is considered ideal for the aged and bad risk patient.

References

1. Saklad, M., and others: Intraspinal segmental anesthesia; preliminary report. Anesthesiology **8**:270 (May) 1947.

2. Tuohy, E. B.: Use of continuous spinal anesthesia utilizing ureteral catheter technic. J.A.M.A. **128**:262 (May 26) 1945.

3. Adriani, John: Pharmacology of anesthetic drugs. Springfield, Illinois, Chas. C Thomas, p. 27, 1947.

4. Wasmuth, C. E. and Hale, D. E.: Continuous spinal anesthesia in the poor risk and aged surgical patient. Cleveland Clin. Quart. **18**:93 (April) 1951.

5. Ansbro, F. P. and Pico, L. J.: Continuous spinal anesthesia; report of 100 cases in which this method was employed. Am. J. Surg. **55**:504 (March) 1942.

PROSTATE GLAND BIOPSY

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THE incidence of cancer of the prostate gland among men who have symptoms of bladder neck obstruction is about one out of five. The actual incidence of cancer is higher because many men are seen with symptoms unrelated to the urinary tract, such as bone pain, or who have evidence of the tumor without symptoms. It is the third most common cancer in men, exceeded only by cancer of the skin and alimentary tract in frequency of recognition.

The chief methods by which a physician discovers prostatic cancer are rectal palpation of the gland, serum acid phosphatase determination, and roentgenographic study of the urinary tract and skeleton. These are satisfactory when the tumor has spread widely beyond the prostate. In this paper methods of biopsy for establishing the diagnosis when cancer of the prostate gland is suspected or when it is desirable to corroborate the clinical diagnosis of extensive cancer will be discussed. The actual diagnosis of cancer is made by microscopic definition, preferably on a block of tumor tissue. Under study is the cytologic examination of prostatic secretion for exfoliated tumor cells,[1] which requires a great deal of time and experience.

Methods of Biopsy

A. **Perineal.** Exposure of the prostate gland through the perineum permits biopsy of any area of the gland which has been suspected of malignancy on rectal palpation. This approach is particularly useful because more than 90 per cent of all prostatic neoplasms arise in the posterior lobe accessible to rectal palpation. The reason for biopsy of such suspicious areas is to offer the patient an opportunity by total prostatectomy for complete removal of an early cancer or assurance of the benign nature of the lesion.

Patients are selected for perineal biopsy chiefly on the basis of rectal findings of an area of nodularity and induration within the confines of the gland. The size of the gland means little because cancer has a development independent of benign enlargement. Evidence of metastasis on physical examination, roentgenographic study of the bones, or elevation of the serum acid or alkaline phosphatase are contraindications to operative perineal biopsy. A plain film of the pelvis will exclude prostatic calculi as the cause of induration within the gland. History of chronic prostatitis or genitourinary tuberculosis may influence the necessity for biopsy. Men who have a poor life expectancy from the age or health standpoint are not considered suitable candidates for perineal biopsy and possible radical prostatectomy. It is not suggested that every pros-

tate with slight irregularity should be biopsied. Many patients with prostatic irregularity not initially suggestive of cancer can be reexamined at intervals for change.

With the prostate exposed perineally, a suitable block of tissue is removed from the area under suspicion and submitted to the pathologist for frozen section. Frequently, cancer can be suspected when the fragment presents both induration and yellowish surface color. With the frozen section technic utilized by Dr. John B. Hazard[2] of the Department of Pathology, accurate correlation between rapid sections and later permanent sections has been attained. Interpretation of prostatic tissue by frozen section is generally considered difficult and unreliable, but use of a method providing differential staining and uniform results is of great value. A portion of each tissue block is used for frozen section and the remainder saved for permanent section. Freezing causes distortion of tissue and use of this second and unfrozen portion permits accurate interpretation of each sample.

With the presence of cancer confirmed by frozen section, the entire prostate gland is separated from the bladder and urethra and removed with adjacent portions of the bladder and genital tract, provided cancer has not spread beyond resectability into these structures. Failure to find cancer on the first frozen section necessitates additional biopsies of adjacent areas of the gland. If these are negative and there is no indication for enucleating obstructing prostatic tissue, the perineal incision is closed and the patient is usually out of the hospital within three to four days.

Over a two year period, 40 men were subjected to open perineal biopsy because of suspected early cancer. Twenty-two were proved to have benign conditions causing the induration. Chronic prostatitis and acinar hyperplasia are the main lesions simulating carcinoma. There were no complications among this group. Eighteen men of this group of 40 were found to have cancer. Of these 18, four were shown to have spread of the tumor into the bladder base, urethral bulb, or laterally, and therefore had biopsy only. Fourteen men had total prostatectomy, ten of whom are believed to have a good chance of complete removal of the cancer based on the pathologic examination of the prostate. The remaining four were found to have carcinoma at the line of excision from the bladder base, discovered only after removal of the gland.

The effect of estrogenic hormones prior to biopsy often leads to confusion. It has been generally accepted that prostatic cancer softens under the influence of estrogens. This is often true of suspected early lesions, making the selection of a proper area for biopsy difficult at operation. Not all malignant nodules soften, however. Figure 1 illustrates a section of a totally removed prostate from a man who was treated with estrogens for a year. The original nodular area did not change significantly in size or consistency during this time. It should be noted that estrogens did not alter the malignant appearance of the tumor microscopically.

The extent of prostatic cancer is best evaluated prior to estrogenic therapy. Alteration of the hardness of tumor spread beyond the prostate with such

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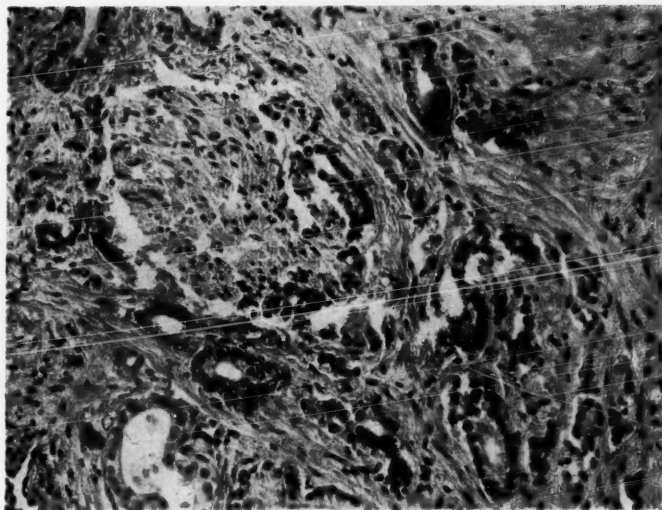
Fig. 1. Adenocarcinoma of prostate gland. Estrogen therapy for one year prior to total prostatectomy. Note perineural lymphatic involvement.

treatment may convey the impression that total prostatectomy will remove all cancer. Complete destruction of tumor cells with hormones does not occur. When a patient is fortunate enough to have a localized prostatic neoplasm diagnosed, the original plan of treatment is most important. Measures should be taken promptly for biopsy and extirpation of these potentially curable tumors.

B. **Needle Biopsy.** A practical method of securing prostatic tissue for pathologic examination without operation is often desirable to corroborate the clinical impression of cancer. The prostate is accessible to needle biopsy by puncture of the perineum, a finger in the rectum guiding the needle into the desired part of the gland. This is done under analgesia, often in conjunction with a cystoscopy. A Silverman needle is used, although there are several other types of prostate biopsy devices available. Several pieces of tissue 0.5 to 1. cm. long can be obtained from various parts of the gland or perineum. It has been noted that the most satisfactory specimens for biopsy are obtained when carcinoma is present; the least satisfactory when the prostate is small and fibrotic. No complications have arisen and there is no morbidity connected with the procedure. Should bleeding occur, digital pressure against the prostate and perineum for a few moments will suffice to control it.

During the same two-year period, 41 such needle biopsies were performed. Of 33 men who were considered clinically to have prostatic cancer, the diagnosis was confirmed by biopsy in 29. There were four false negative biopsies of men who had metastases demonstrable by x-ray or later operation. This illustrates

the well known fact that a negative biopsy is meaningless and should not influence the course of treatment under such circumstances. Eight men who had clinically benign prostate glands or metastatic tumor from other sites surrounding the genital structures, had prostate biopsy specimens which showed no evidence of malignancy.

For the purpose of perfecting and evaluating this method of needle biopsy, many patients with extensive metastases and abnormal serum phosphatase levels were utilized. Biopsy is not considered essential in such instances, however a satisfactory needle biopsy will provide sufficient tissue to distinguish adenocarcinoma from an undifferentiated carcinoma. This may be of some value in anticipating the result of estrogenic therapy. Biopsy corroboration of prostatic cancer has been particularly useful when metastases are present in an unusual form, as in the following case report:

A 53 year old man was admitted to the hospital, having been bedridden with back pain, weight loss and nausea. The pain in the dorsal area began three months previously. Physical examination disclosed only tenderness over the spine. Roentgen study revealed compression fracture of D6 and D8 vertebrae, and osteolytic metastasis in the right scapula, ribs and iliac bones. The acid phosphatase was 1.5 B.U. Sternal marrow biopsy disclosed adenocarcinoma; following this the prostate gland was reexamined. It was small with a firm upper border joining the bladder base, from which hard cords of tissue extended laterally to the walls of the pelvis. Needle biopsy of the prostate was performed disclosing adenocarcinoma (fig. 2). Immediate weight gain and relief of pain followed institution of estrogenic therapy.

Carcinoma of the prostate usually causes osteoblastic metastases and in this man the bone lesions were destructive. The serum acid phosphatase is elevated in approximately two thirds of all patients with osseous metastases of prostatic origin;[3] serum acid phosphatase value of 1.5 B.U., such as in this case, is not considered abnormal.

C. **Transurethral Biopsy.** Since most prostatic neoplasms develop in the posterior part of the gland, transurethral resection often fails to go deep enough to secure representative tissue from this portion. Unless there is evidence of pathologic change or tumor extension around the vesical neck or into the prostatic urethra cystoscopically, biopsy by this means is usually inadequate. Its usefulness should not be overlooked under appropriate circumstances such as the following case:

A 35 year old man entered the hospital with chills, fever, dyspnea, and abdominal masses of one month's duration. One episode of acute urinary retention occurred followed by frequency and urgency. There were rales in both lungs, a large spleen, and an enlarged firm right lobe of the prostate gland. Chest x-ray showed patchy infiltration of both lungs. Abdominal film showed localized inflammatory changes in the 12th vertebral body, and a large splenic shadow with displacement of the left kidney downwards. The urogram revealed normal kidneys but the bladder base was indented, consistent with a large prostate. The hemoglobin was 9.8 Gm. per hundred cubic centimeters; urine was loaded with pus cells, red blood cells, and showed albumin; it was sterile on culture. The urine, gastric washings, and sputum were all negative for acid fast bacilli. PPD. was negative on first strength but positive on second strength. Cysto-

scopy revealed elevation of the posterior commissure; several pieces of tissue were removed from this area with the resectoscope. These showed active caseating tuberculosis.

The differential diagnosis in this man was between Hodgkin's disease and tuberculosis. Transurethral biopsy of his abnormal prostate gland proved a simple and efficacious means of establishing the diagnosis.

Summary

1. Three methods of prostatic biopsy are described with their indications and limitations.

2. The results of 81 prostate gland biopsies are presented. There were 40 open perineal biopsies in men suspected of having localized prostatic cancer. Twenty-two of these showed no evidence of cancer on biopsy; 18 demonstrated cancer on biopsy and appropriate surgical measures were taken wherever possible. There was an accurate correlation between the frozen and permanent sections in all instances.

Forty-one perineal needle biopsies were done during the same period. Of 33 men known to have metastatic prostatic cancer, 29 biopsies showed cancer and four did not (false negative). The eight remaining patients were not considered to have prostatic cancer and had negative biopsies.

3. Transurethral biopsy of the prostate is usually inadequate unless there is evidence of pathologic change along the urethra.
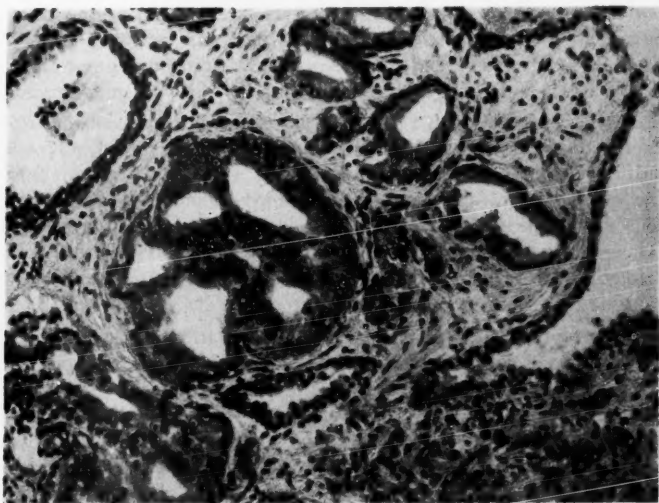
FIG. 2. Adenocarcinoma of prostate gland. Specimen secured by needle biopsy. Note reduplication of lumina and nuclear dedifferentiation.

4. Open perineal biopsy is the preferred method of accurately establishing the diagnosis of localized prostatic cancer, and is necessary for histologic confirmation prior to radical prostatectomy. Chronic prostatitis and acinar hyperplasia often simulate cancer on rectal palpation.

5. Needle biopsy is a useful means of obtaining tissue for histologic confirmation of metastatic prostatic cancer, particularly when the metastases are of an unusual nature. It is not accurate enough to use with localized lesions nor is it adaptable to frozen section technics.

References

1. Peters, H. and Young, J. D.: Prostatic smear in cancer diagnosis. J.A.M.A. **145**: 556 (Feb. 24) 1951.
2. Hazard, J. B. and Stevenson, G. F.: A frozen section technic. Am. J. Clin. Path. **19**: 873 (Sept.) 1949.
3. Nesbit, R. M. and Baum, W. C.: Serum phosphatase determinations in diagnosis of prostatic cancer. J.A.M.A. **145**: 1321 (April 28) 1951.

THE THERAPEUTIC BASIS OF BREATHING EXERCISES

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THE value of breathing exercises has not been sufficiently stressed in the past. Most physicians have not been trained to think in terms of prescription of therapeutic exercise as they have in prescription of drugs or in indications for operative procedures. However, with the introduction of courses of physical medicine and rehabilitation into the curricula of many medical schools, encouraging progress is being made in giving younger physicians a basic understanding of therapeutic exercise. It is hoped that with this new emphasis, greater use will be made by all physicians of such simple yet beneficial procedures as breathing exercises in conditions where they are indicated.

Three conditions in which breathing exercises have proved to be of definite value will be discussed. Special consideration will be given to the pathologic physiology present in each instance, particularly in so far as it affects respiration, and to the therapeutic objectives of breathing exercises. The exercises themselves will be outlined briefly in the form that has been found most practical for instruction of patients.

Physiology of Normal Respiration. Since the rationale for breathing exercises is based upon physiologic principles, a brief discussion of the physiology of normal respiration is warranted. Respiration in a strictly physiologic sense is the exchange of oxygen and carbon dioxide between living cells and their environment. However, the term respiration usually refers to the movements of inspiration and expiration which provide an intermittent flow of air through the lungs sufficient for the exchange of the respiratory gases.

In quiet respiration, inspiration is the active process, carried out primarily by contraction of the diaphragm and, to a lesser extent, of the lower external intercostal muscles. The increase in size of the thoracic cavity resulting from descent of the dome-shaped diaphragm, and lateral flaring of the lower thorax, creates a negative pressure which allows air to inflate the easily distended lungs. Expiration, conversely, is almost entirely a passive process in quiet respiration, depending upon the elasticity of the lungs and the force of gravity to expel the air and return the expanded thorax to its neutral position.

In forced inspiration such as occurs after strenuous exercise, the diaphragm is still the most important muscle, accounting for about 60 per cent of the vital capacity. However, in such a situation accessory respiratory muscles act to supplement the action of the diaphragm and to increase the amount of air inspired by elevating and bringing forward the sternum. Other accessory muscles enlarge the nostrils, spread the vocal cords, and adapt body posture for maximal inspiration. The following are accessory muscles of inspiration: external intercostal, sternocleidomastoid, scalene, trapezius, pectoralis minor, serratus posterior, dilator naris, erector spinae and rhomboid muscles.

In forced expiration another group of accessory respiratory muscles act to compress the thorax and thus to expel a stream of air in a manner not unlike the action of bellows. In forced expiration there may be also an adaptation of body posture to allow maximal expiration by slight flexion of the dorsal spine, slumping forward of the shoulders and stabilization of the arms. The accessory muscles of expiration are the following: rectus abdominis, internal and external oblique abdominal, internal intercostal, latissimus dorsi, serratus anterior, pectoralis major, deltoid (lower fibers), and quadratus lumborum muscles.

When breathing quietly certain persons, more commonly women, make use of upper thoracic and intercostal muscles rather than the diaphragm. An important factor here is probably the wearing of tight-fitting girdles and corsets which prevents normal expansion of the abdomen in inspiration. Some women seem to have forgotten how to use the diaphragm correctly. Since they are already utilizing their "reserve" respiratory muscles for quiet breathing, they have reduced tolerance to exercise. In advanced cases, faulty breathing may cause symptoms such as fatigue, breathlessness, difficulty in climbing stairs, tachycardia and lightheadedness. Patients with these complaints occasionally are diagnosed as having neurocirculatory asthenia, effort or hyperventilation syndromes.

The amount of air breathed in and out during quiet respiration is approximately 500 cc.; this is called "tidal air." The total amount of air that a person can take into his lungs in deep inspiration and breathe out in forced expiration is called "vital capacity"; the average vital capacity of an adult is about 4000 cc.

It is unnecessary to discuss in detail the regulation of respiration by the nervous system. Respiratory movements are both voluntary and involuntary. Normally, however, respiration is almost entirely an unconscious process determined by automatic activity of the cells of the respiratory centers in the medulla, which are in turn influenced by certain chemical and reflex factors. Each respiratory center in the medulla consists of an inspiratory and an expiratory center. The inspiratory center originates impulses which cause contraction of the diaphragm and the accessory muscles of inspiration. The inspiratory phase of respiration continues until a sufficient number of inhibitory impulses arrive at the inspiratory center from either the expiratory center or through the vagus nerve from stimulated nerve endings in the distended alveoli (Hering-Breuer reflex). The inspiratory center is specially sensitive to amounts of carbon dioxide in the blood slightly in excess of normal, which result in an intensified shower of impulses from the center to the inspiratory muscles. The carotid body and carotid sinus structures in the neck, although also sensitive to changes in carbon dioxide content of the blood, play a negligible role in the regulation of normal respiration.

Respiration is easily inhibited reflexly by a wide variety of stimuli: coughing, sucking, talking, swallowing, sudden pain, or a whiff of sulfur dioxide, to men-

tion a few examples. Respiration is also influenced in a variety of ways (e.g. in rate, depth, and rhythm) by certain emotions or mental attitudes, such as laughter, crying, interest, rage and fear. From this consideration it is apparent that there must be many subcortical reflex connections involved in the control of respiration.

Indications for Breathing Exercises

Breathing exercises are prescribed in a number of medical and surgical conditions. They are employed ordinarily for one or more of the following purposes: (1) to increase vital capacity; (2) to abort asthmatic attacks; (3) to prevent or to correct postural abnormalities; and (4) to gain better control over respiratory movements.

Rheumatoid spondylitis is a disease in which increasing the vital capacity is of paramount importance. In asthma, breathing exercises are prescribed both for the purpose of increasing the vital capacity and aborting acute attacks. Prevention and correction of postural abnormalities are important in both rheumatoid spondylitis and asthma, and in the postoperative care of patients who have had thoracic surgery. Following thoracic surgery it is also important to reeducate the patient to breathe correctly using both sides of the thorax equally.

Intercostal Breathing in Rheumatoid Spondylitis. Rheumatoid spondylitis is a systemic disease of unknown etiology which runs a chronic, progressive course over the years but which may undergo remissions and exacerbations. Although it is a systemic disease similar in many respects to rheumatoid arthritis, the major manifestations of rheumatoid spondylitis occur in the joints of the spinal column, particularly the sacro-iliac and the small intervertebral and costovertebral articulations.

The pathologic process begins as a synovitis with exudation into the joint cavity and erosion of the cartilage. The joint cavity is eventually obliterated by fibrous connective tissue and finally, after a period of a few years, by bony ankylosis. Osteoporosis of the vertebral bodies and calcification of the longitudinal spinal ligaments also occur.

Physicians are familiar with the tragic picture of the untreated patient with rheumatoid spondylitis in whom the pathologic process has run its course. His spine is bent forward in a position of pronounced kyphosis and he is completely unable to straighten up. With his head held forward and his chin depressed toward his flattened chest, he is unable to turn his head more than a few degrees in any direction. His thoracic cage is fixed in a position of expiration, permitting him to breathe only with his diaphragm.

There are many measures that are important in the treatment of rheumatoid spondylitis: roentgenographic therapy, orthopedic procedures and braces, use of heat, exercises, drugs such as cortisone, and limitation of activities. None of these is more important, however, than intercostal breathing and postural exercises. Such exercises are more effective in the early stages of rheumatoid spondylitis and are prescribed to increase the breathing capacity by mobilizing the thorax and to maintain or obtain posture as nearly normal as possible by strengthening the erector spinae and rhomboid muscles and stretching the pectoral muscles. So easily do these exercises supplement one another that it has

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been found convenient to combine them into simple routines for instruction of patients with rheumatoid spondylitis. The following exercises should be taught these patients:

1. Lie on your back on a firm surface without a pillow under your head. Clasp both hands under your head and pull your elbows firmly downward while inhaling deeply. Hold this position for five seconds, then exhale and relax. Repeat 5 to 20 times.
2. Lying on your back, place a rolled towel between your shoulder blades. Inhale slowly and raise your arms upward and back over your head as far as possible; then exhale and lower arms to sides. Repeat 5 to 20 times.
3. Lie on your abdomen. Stretch your arms outward at the sides to shoulder level. Raise your head, chest, shoulders and arms off the bed. Relax and repeat 5 to 20 times.
4. Stand facing the corner of a room at arm's length from the walls. Place one hand on each wall at shoulder level. Bend elbows slightly and hold abdomen in. Slowly let the weight of the body go forward forcing the chest toward the corner, at the same time inhaling deeply. Return to original position and exhale. Relax and repeat 5 to 20 times.
5. Suspend the body without bending elbows by grasping an overhead bar with hands width of shoulders apart. Except for clenched hands, remain as relaxed as possible for five seconds. Rest, and then repeat 5 to 10 times.

The patient is instructed to do each of the foregoing exercises several times each day, and gradually increase the repetitions. Special instruction is necessary to acquaint the patient with correct posture and to impress upon him that he must always be "posture conscious." He will be most comfortable sleeping upon a firm mattress with a board underneath and sitting erect in firm, straight back chairs. Finally, the patient is advised to measure both his chest expansion and his height every month so that he will be aware of his progress in the program of exercises.

Diaphragmatic Breathing in Asthma. In contrast to rheumatoid spondylitis where limitation of inspiration is the major problem, the primary difficulty in asthma occurs during expiration. Often a paroxysmal attack of dyspnea occurs without warning within a few minutes in an asthmatic patient; such an attack is first manifested by a feeling of oppressive tightness over the chest. Even though the patient employs his accessory respiratory muscles during an attack, little excursion of the thorax actually takes place. The acute attack may last from 15 minutes to several days, and is usually of milder intensity in attacks of longer duration.

Although the underlying cause of asthma is not established, the mechanism of the asthmatic attack seems to be generally understood. It is believed that an attack is initiated by generalized spasm of the smooth muscle in the finer bronchioles, followed by edema of the mucosa and accumulation of secretion. This process creates a barrier to escape of air from a considerable portion of the pulmonary alveoli, thereby making it extremely difficult for the patient to exhale. However, upon deep inspiration he can often slightly enlarge the constricted lumina of the bronchi, allowing additional air to enter the already expanded alveoli; this action might be compared to that of a ball valve. During an

asthmatic attack, the lungs become overdistended, or emphysematous and the thorax is kept in a position of partial inspiration. As the acute attack subsides, both the lungs and the thoracic cavity eventually return to normal size.

In the patient who has suffered from asthma for many years, the attacks gradually increase in duration and chronic changes occur in the lungs and thorax that are not reversible. The thorax gradually assumes a barrel shape, adapting itself to the secondary emphysema; widening of the costal angles and Harrison's grooves may also appear. The patient has a musical, wheezing respiration and must utilize his accessory muscles. He frequently has a chronic productive cough.

The objectives of breathing exercises for the asthmatic patient are the following: (1) to re-educate the patient to use his diaphragm more effectively in quiet respiration, rather than his upper thoracic accessory respiratory muscles; (2) to increase vital capacity; (3) to restore the enlarged chest to proportions as nearly normal as possible and, in the younger asthmatic patients, to prevent such enlargement; (4) to abort asthmatic attacks.

Most programs of breathing exercises follow the routine outlined by the Asthma Research Council of Great Britain. These exercises are usually begun with the patient in a supine position. Later they may be supplemented with exercises in a sitting or standing position, which should be done before a mirror if possible. Before starting the exercises, the patient should clear his airway by blowing his nose. The following are the basic breathing exercises taught asthmatic patients:

1. (a) Lie on your back with head and knees comfortably supported by pillows. Take in a breath through your nose and then exhale slowly through the mouth, making an "f" or "s" sound. Gradually try to increase the length of the time you are able to make this sound in one breath. However, it is most important not to prolong the sound to the point where you must gasp for a new breath. Repeat three times.

   (b) Learn to keep the upper part of the chest still when inhaling so that inspiration is carried out mainly by the diaphragm. When exhaling, the abdominal muscles should contract, sinking in toward the spine. Then let the next breath drawn into the lungs come automatically, so to speak, by simply allowing the abdominal wall to relax (or swell).

   (c) Unless the chest is absolutely clear, exhale during the preceding exercises just sufficiently to hear wheezing noises in the bases of your lungs. This may cause coughing and increased wheezing at first but keep trying gently as it will soon be possible for you to do this exercise without distress.

2. Sitting on a chair, preferably in front of a mirror, wrap a wide belt at least five inches in width once around your lower ribs above the waist. Holding onto the ends of this belt, breathe out slowly, sinking first the upper chest, then the ribs, and finally compressing the ribs by tightening the belt. Then while breathing in quietly, feel the lower ribs expand against the pressure of the belt. Repeat five times.

A number of exercises are often added for the asthmatic patient, but these are concerned more with the correction of faulty posture than with the mechanism of respiration. The foregoing exercises should be done each day for at least

10 and gradually increasing to 20 minute periods at the following times: (a) before breakfast when the patient feels fresh and is least likely to be dyspneic; (b) at night before retiring, to clear the lungs in preparation for sleep; and (c) at the first sign of an impending attack, in order to avoid it if possible. Also the patient should practice diaphragmatic breathing frequently throughout the day. It is advised that the patient perform the exercises for three months, at the end of which time he may decrease to five minute periods twice daily for the next 12 months.

Breathing Exercises Following Thoracic Surgery. Extensive experience was gained during World War II in the treatment of patients with chest injuries. Thoracic surgeons were quick to realize the tremendous help that intensive rehabilitation programs could give to their patients. An important part of the rehabilitation program for these patients consists of breathing exercises, the purposes of which are the following: (1) to prevent adhesions from forming between visceral and parietal pleura that might limit movement of lungs and ribs; (2) to instruct the patient in correct breathing and thus to prevent any postural abnormalities that might result from faulty breathing; and (3) to strengthen accessory muscles of respiration that had been severed during surgery.

Breathing exercises have an important role in the preoperative preparation of the patient for elective thoracic surgery as well as in the postoperative management. It is customary to begin diaphragmatic breathing exercises as soon as possible following surgery in order to prevent the formation of adhesions. However, because of postoperative pain it is difficult if not impossible to instruct the patient adequately in such exercises after the surgical procedure has been carried out. Therefore, it is advisable to instruct the patient before surgery in the breathing and postural exercises that will be instituted later. He should also be informed before the operation of the amount of pain and disability that he can expect, and of the importance of maintaining good bed posture and doing the exercises prescribed throughout the convalescent period.

Following surgery the patient will invariably splint the side involved and breathe with the normal side of his chest. At first this unilateral breathing requires conscious effort but soon becomes automatic. The day following surgery the patient should be encouraged to do the diaphragmatic breathing exercises if possible. It is important to instruct the patient in proper positioning in bed. If these measures are not given careful attention, the classic deformity that has been known to follow thoracic surgery may develop: tilting of head toward affected side, lowered shoulder on same side with a tendency for it to ride forward, and fixation of diaphragm in a position of full expiration on the involved side. Later in the postoperative period, careful re-education of the muscles of respiration and intensive postural training must be instituted.

Re-education of the respiratory muscles is often required to get the patient to breathe correctly with both sides of his chest. Two exercises that may be used

to make the patient aware of the function of the respiratory muscles follow: the first of these exercises may require a considerable amount of supervision.

1. Lying supine in bed, place hands over lateral chest on involved side. Take in as deep a breath as possible, maintaining gentle pressure on the hands throughout inspiration. Hold for a count of three and exhale. During expiration apply greater pressure on your chest than during inspiration; at the end of expiration, give a sudden thrust to your hands and release. Repeat five to ten times, twice daily.

2. Lying supine in bed with knees drawn up, place hands on lower margin of ribs anteriorly. Take a deep breath and feel the abdomen swell under your hands and the ribs pull wider apart. Hold for count of three. Now exhale slowly, allowing the upper chest to sink lower, and then the upper abdomen. Repeat five to ten times, twice daily.

In addition to these exercises, postural exercises are of great importance following thoracic surgery; these are directed at making the patient aware of correct posture and at mobilization of the neck and the shoulder girdle. The progress made in re-education of respiratory muscles can be evaluated through periodic fluoroscopic examinations.

Conclusions

1. Breathing exercises have an important place in treatment of rheumatoid spondylitis and asthma and in the preoperative and postoperative management of patients who are to have thoracic surgery.

2. In rheumatoid spondylitis, breathing exercises are carried out to increase intercostal expansion and the depth of inspiration.

3. In asthma, breathing exercises are prescribed which stress contraction of the diaphragm and increasing the expiratory phase of respiration.

4. In the management of patients who are to have thoracic surgery, breathing exercises are of value in preventing pleural adhesions, asymmetrical respiration and postural deformities.

5. The utilization of breathing exercises in the cited instances is based upon sound physiologic principles.

References

1. Asthma Research Council: Physical exercises for asthma. 7th Ed., King's College, Strand, London WC 2, pp. 26, 1947.

2. Best, C. H. and Taylor, N. B.: The physiological basis of medical practice. 4th Ed., The Williams & Wilkins Co., 1945.

3. Harken, D. E.: Review of activities of thoracic center for III and IV hospital groups. 160th General Hospital, European Theater of Operations. June 10, 1944 to Jan. 1, 1945. J. Thoracic Surg. 15: 31-43, 1946.

4. Krusen, F. H.: Physical medicine and rehabilitation for the clinician. Chapter by Polley, H. F.: Rheumatoid spondylitis — Clinical features and methods of treatment. pp. 166-175. W. B. Saunders Co., Philadelphia, pp. 371, 1951.

CHANGES IN SURGERY FOR CARCINOMA OF
THE STOMACH
1940 through 1951

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CARCINOMA of the stomach continues to be a most perplexing problem both from diagnostic and therapeutic standpoints. Too often the cancer has been present so long and has spread so insidiously that removal is impossible. Wangensteen[1] estimates that the usual neoplasm has been present for 20 months before it causes any symptoms, and that six months elapse before the symptoms are sufficiently severe for the patient to see a doctor. It is not surprising that the most favorable reports show a resectability rate of only 50 to 60 per cent of these long existing lesions and that the five year survival rate is so low.

Several new developments in the surgical attack on gastric cancer have occurred during the past 10 to 15 years and may influence the outlook for the patient with carcinoma of the stomach. These changes have been: (1) Tissue diagnosis has replaced "clinical judgment" regarding operability; (2) It has been realized that operability cannot be determined by roentgen examination of the stomach; (3) Extension into the esophagus is no longer regarded as a contraindication to operation; (4) Extension into neighboring organs is not a contraindication to operation; (5) As has been indicated by Guiss,[2] "There is an increasing tendency to determine true resectability by laparotomy;" (6) Total gastrectomies have been advocated for carcinoma of Borrmann's type IV by some[1] and for all carcinomas of the stomach by others.[3,4,5,6,7] More recently Lahey[8] stated that he did not believe that total gastrectomy was indicated for the low prepyloric or antral lesions; (7) Wangensteen[1] has discussed the idea of "second-look" operations and McNeer et al.[9] have reported operations for recurrent gastric carcinomas.

We believe the preceding factors, reflecting a more aggressive approach to gastric cancer, will result in increased five year survival rates. We, as gastroenterologists and internists, are interested in the changes in surgery for cancer of the stomach, and in what affect these changes may have on the prognosis of the patients we observe with gastric carcinoma. Should the internist refer all his patients with gastric cancer to the surgeon, or should he select the ones to be referred? We attempt to show in this article the change in surgical approach to the patient with gastric cancer from the years 1940 through 1945 to the present time.

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1. Results of Surgery for Cancer of the Stomach 1940 Through 1945

The passage of time enables us to evaluate our diagnoses and treatment of gastric carcinoma in the years 1940 through 1945. These results have been published in more detail elsewhere,[10] but will be briefly reviewed.

Table 1

OPERABILITY, RESECTABILITY, AND CURABILITY
1940 through 1945

Group	No. of Patients	Per cent of Total Group	5 Year Survival
Resection performed	100	25	27 (6.6% of total group)
Palliation and exploration	135	33	0
Operation refused	44	11	0
Inoperable	127	31	2
TOTAL	406	100	29 (7.1% of total group)

Four hundred and six cases of carcinoma of the stomach were seen from 1940 through 1945. The resectability rate was 25 per cent (table 1). Palliative surgery or exploration only was performed in 33 per cent. Eleven per cent of the patients refused surgery. The percentage considered operable, including those who refused surgery, was 69 per cent of the total, although only 58 per cent were operated upon. Of the 235 patients operated upon, 43 per cent had gastric resections.

There were 29 five year survivals; two patients surviving for five years without surgery. One of these patients was considered inoperable in 1945 because of the extent of the disease disclosed by roentgen examination; he returned with increasing symptoms in 1951 at which time a gastric resection was performed. The other five year survivor without surgery had extension into the esophagus, as determined by esophageal biopsy, and was considered inoperable. It is remarkable that she survived for seven years before succumbing to her disease. Esophageal involvement and extent of the disease as determined by roentgen examination are no longer considered contraindications to operation. Both of these patients would be operated upon today and would be considered five year "cures."

The remaining 27 five year survivors represent 6.6 per cent of all the patients seen with gastric carcinoma from 1940 through 1945, and 27 per cent of those who had gastric resections. Twenty-three are alive and well today. Four have died, all with recurrences of carcinoma. The survival for five to seven years

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after surgery with death following an extension of the original disease certainly indicates that five year survival does not mean five year "cure." The five year survival rate of 7.1 per cent compares favorably with other series of this period. Maimon and Palmer,[11] in reviewing other published series in 1949, stated "The incidence of five year survival in all patients with carcinoma of the stomach varies from 2.1 to 7.5 per cent." Series of cases, including all gastric malignancies such as Hodgkin's disease, lymphoblastomas, and lymphosarcomas of the stomach, should not be compared with series dealing strictly with gastric carcinoma, since the nonepithelial malignancies of the stomach have a much higher five year survival rate than gastric carcinoma, and will favorably affect the overall survival rate for gastric malignancies.

Of the 100 resections, eight were total, and seven were complicated resections in which some other organ was removed at the same time. One patient with extension of the disease to the gallbladder and liver, and another with extension to the tail of the pancreas and hilum of the spleen, are alive and well today. Forty-one per cent of the five year survivals had positive lymph nodes and 22 per cent extension of the disease to neighboring organs, indicating that such lymph node involvement and extension of the disease do not necessarily mean that the patient is nonresectable and noncurable. It should also be noted that a palpable mass was present on physical examination of six of the five year survivors, showing that the presence of a mass is not a contraindication for operation.

The gross pathology of the lesion, as has been reported by others, is of considerable prognostic value. This is presented in table 2. The most favorable prognoses were those for polypoid lesions; 58 per cent of these patients survived. Seventeen per cent of the patients with ulcerating lesions survived, 22 per cent of those with annular lesions survived, and only 13 per cent of those with infiltrating lesions survived. Unfortunately the majority of the lesions are of the type that have a poor prognosis.

Table 2

GROSS PATHOLOGY AND SURVIVAL

Pathologic Condition	Survivals	Died	Total	Per cent Survivals
Polypoid	15	11	26	58
Ulcerating	7	35	42	17
Annular	2	7	9	22
Infiltrating	3	20	23	13

Palliative surgery (gastroenterostomy in 43, gastrostomy in three, loop colostomy in one, and a closure of a perforation in one) was performed in 48 patients, and exploration only in 87 patients: a total of 135 patients. Distant metastases, such as the presence of a Blumer's shelf, peritoneal seeding, and liver metastases, were the indications which made gastric resections inadvisable in 51 patients. Extension to other organs (30 patients), and lymph node involvement in 45 patients were other reasons for not resecting the stomach. We believe that today some of the latter 75 patients would have had resections.

The importance of tissue diagnosis was emphasized by the course of several patients. One had a gastroenterostomy for what was thought to be a penetrating, nonresectable, malignant gastric ulcer. Tissue diagnosis was not obtained. Following the gastroenterostomy, the ulcer healed and has remained healed to the present time. It is obvious that this ulcer must have been benign rather than malignant. Three other patients were considered nonresectable because of omental nodes or peritoneal implants; permanent microscopic sections were negative for tumor cells. Frozen sections, which were not used from 1940 through 1945 as they are at the present time, can be of considerable help to the surgeon in determining the advisability of resection in such questionable cases.

One hundred and twenty-seven patients were considered inoperable. The chief reasons are presented in table 3. Physical examination determined the nonoperability in 63 patients; 20 had fixed masses. This would seem to be a questionable contraindication since six of the five year survivors had masses on physical examination. Hepatomegaly, and even a nodular liver, does not necessarily mean the patient has metastases, but may represent a concomitant cirrhosis. Tissue diagnosis was not usually obtained in these patients in 1940 through 1945.

By roentgen examination the disease was considered too extensive for operation in 25 patients. Two patients so considered, but not included in this series, were treated with small doses of roentgen therapy by their local physicians, and are alive and well today. They obviously did not have carcinoma, but perhaps had hypertrophic gastritis. This again emphasizes the importance of obtaining a tissue diagnosis and the doubtful reliability of determining operability by roentgen examination of the stomach. Esophageal involvement, usually determined by roentgen examination, was the primary reason for not operating on 19 patients. With improvement in surgical technic, esophageal involvement is no longer considered a contraindication to surgery.

We believe if the modern concept of the most extensive possible surgery for cancer had been accepted, 71 of the 127 patients considered inoperable could have been subjected to surgery with at least a chance of a five year survival in a few. Certainly, without gastric resection, their future outlook was hopeless.

Table 3

REASONS FOR NONOPERABILITY

	Number of Cases
Recurrence (previous surgery).............	5
Physical examination	63
Fixed mass 20	
Hepatomegaly 7	
Nodular liver 10	
Blumer's shelf............................ 20	
Ascites................................... 4	
Virchow's node 2	
Roentgen examination	25
Esophageal involvement...................	19
Metastases (distant—x-ray evidence)	14
Gastroscopic examination..................	1
	TOTAL 127

2. Changes in Surgery

The resectability and operability rates (the actual percentage of patients operated upon) for the years 1940 through 1945 and subsequently through 1951 are presented in Chart I. The operability rate in 1940 through 1945 was 57 per cent and rose gradually until it was 82 per cent in 1950, and 86 per cent in 1951.

Similarly, the percentage of patients undergoing gastric resection has increased. Only 25 per cent of the patients had gastric resections in 1940 through 1945, while in 1950 the percentage rose to 51 and in 1951 was 49 per cent. With the resectability rate doubled, there is a much greater chance for salvage and for five year survival than in the former years.

Other changes in the surgical approach to gastric carcinoma are illustrated in Chart II. Total resections have increased from 2 to 9 per cent. Total resection is not performed routinely, as has been advocated by some, but is done for any lesion, usually scirrhous and infiltrating, demanding entire removal of the stomach for adequate normal gastric margin. Complicated resections, in which some other organ such as the spleen or pancreas had to be removed at the same time, increased from 2 to 15 per cent. We believe that this is most important, since we have shown that some patients have been five year survivors even

OPERATIONS AND RESECTIONS
1940-1951

PER CENT
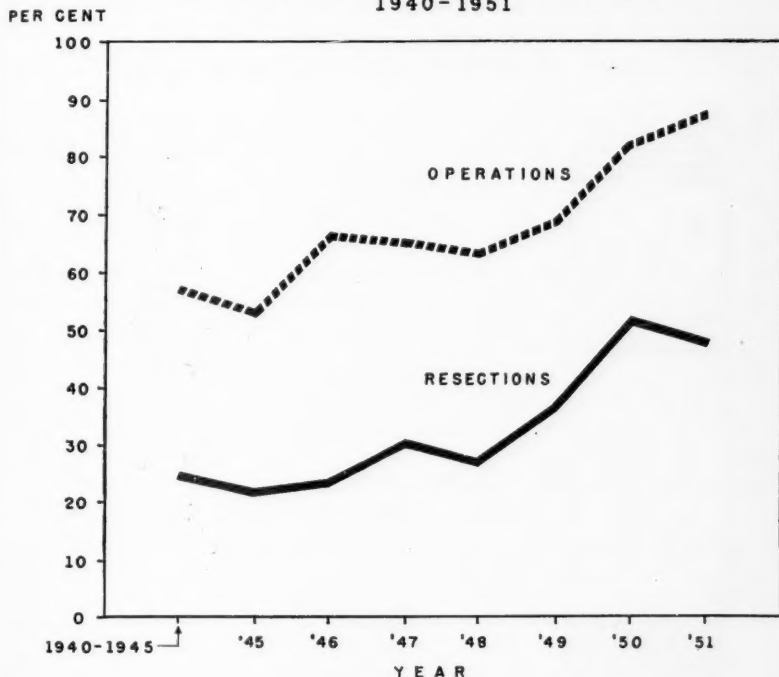
Chart I

though they had extension of the disease to some other organ at the time of operation.

Postoperative mortality has not changed appreciably during this period. From 1940 through 1945, 406 patients with gastric carcinoma were seen; 100 patients underwent resections with nine postoperative deaths, a mortality rate of 9 per cent. In 1950 and 1951, 170 patients were seen; 84 underwent gastric resections with eight postoperative deaths, a mortality rate of 9.5 per cent. Many of the eight patients who died following gastric resection had extensive involvement and probably would not have been five year survivors. At the present time, more extensive surgery is being performed, more total resections, and more complicated resections when the disease has extended beyond the stomach to other organs. There has been no increase in postoperative mortality rate.

The percentage of resections among those patients with gastric cancer whom we observed has increased from 25 per cent to 49 per cent. The per-

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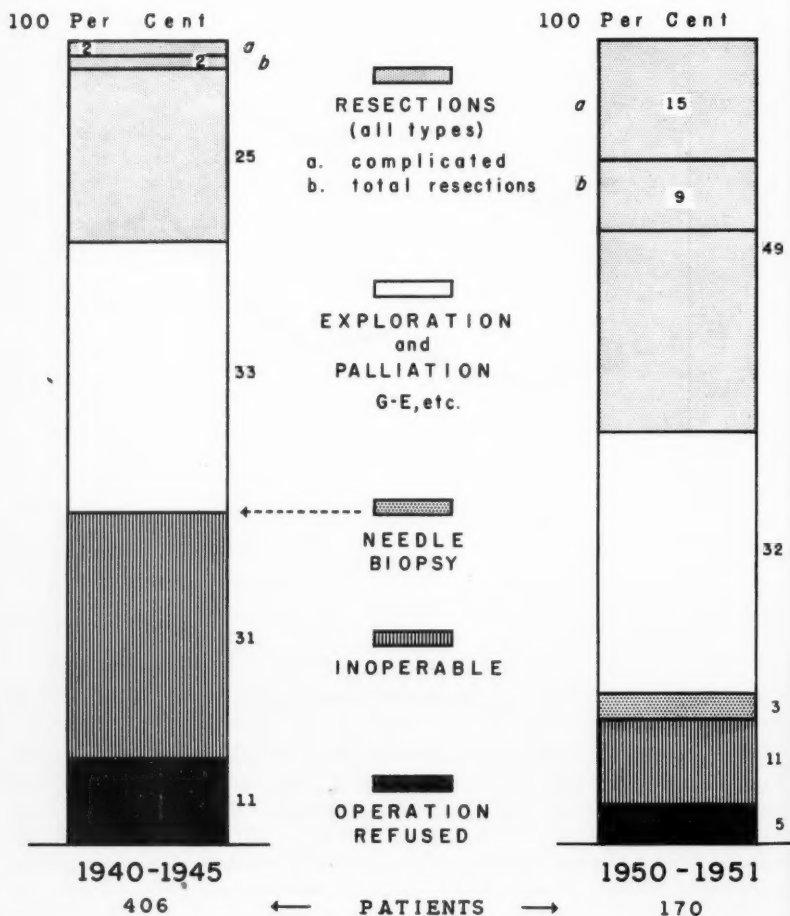
Chart II

centage of patients subjected to exploration or palliative procedures has remained about the same. There is one difference, however; at the present time a biopsy specimen is always taken which was not done in 1940 through 1945. The percentage of patients considered inoperable has decreased from 31 to 11 per cent.

Needle biopsy of the liver and of a Blumer's shelf was not employed in 1940 through 1945, but resulted in a tissue diagnosis in 3 per cent of the patients in 1950 through 1951, without resorting to an exploratory operation. One patient with a Blumer's shelf and three patients with nodular livers had needle biopsies, all of which were positive for carcinoma. The importance of needle biopsy, or exploration to obtain a tissue diagnosis, cannot be overemphasized. There is always the possibility that the lesion may actually be a lymphoblastoma sensitive to roentgen therapy. This has already been stressed, and is aptly illustrated by two other patients. Both of these patients had gastric lesions thought to be carcinoma; one had a supraclavicular node and the other patient had a metastatic lesion in a rib. Biopsy of the supraclavicular node and the rib lesion disclosed that the patients actually had lymphoblastomas sensitive to roentgen therapy. It is quite possible that in earlier years these two patients would have been considered inoperable, that a diagnosis of carcinoma with metastases would have been made without a tissue diagnosis, and they would have been deprived of the years that roentgen therapy may give them.

While this paper is concerned only with carcinoma, actually 7.1 per cent of the malignant gastric lesions seen in 1950 through 1951 were nonepithelial tumors, not carcinoma, and hence are not included in these figures. Many of these mesenchymal tumors are radiosensitive. Without a tissue examination, accurate diagnoses of these patients are not made. They do not receive the benefit of all available therapeutic measures, such as roentgen therapy, nitrogen mustard and similar treatment. Biopsy of a supraclavicular node, an enlarged or nodular liver, a rib metastases, or examination of the ascitic fluid for cancer cells should always be made before the patient is considered hopelessly incurable.

Eleven per cent of the patients in 1940 through 1945 refused operation, while in 1950 through 1951 this number was reduced to 5 per cent. We believe that proper explanation of the problem to the patient can further reduce the number of patients refusing surgery to a minimum. It is unfortunate that so many doctors (at the insistence of relatives of the patient) hide the diagnosis of cancer from the patient. Most patients can accept such a diagnosis and adjust to it more easily than they can adjust to continued worry and doubt. When they are not told the diagnosis, they continue to feel ill, know that they are not well, and may go from one clinic to another, from doctors to faith healers and other quacks. When they know the truth they can accept whatever procedures are required or recommended by the physician or surgeon who understands the problem. It has been our experience that most patients prefer that the doctor be honest with them. Today there should be *no* patient refusing operation for gastric cancer.

We believe that the present surgical attack on gastric cancer can increase the five year survival rate to 15 per cent. Wangensteen[1] has already reported a five year survival rate of 12.2 per cent, and Pack and McNeer[12] have reported 12.3 per cent "cures." Berkson, Walters, Gray and Priestley[13] estimated and predicted a five year survival rate of 14 per cent for all patients with gastric carcinoma who were seen at the Mayo Clinic from 1940 through 1949; their figure is only an estimate since it has not been five years since all of their patients were operated upon, and since they assume that "none of the patients who did not undergo resection are living five years afterward." Such an assumption can be false, since we had two five year survivors without any surgery. We hope to be able to report in the future a five year survival rate of 15 per cent with the present aggressive surgical attack on gastric carcinoma.

Another new factor in the treatment of gastric cancer is the "second-look" operation[1] and operations for recurrent gastric carcinoma.[9] One patient in our group was particularly interesting. In 1941 a subtotal gastric resection was performed for a carcinoma of the antrum. This patient returned in 1949 with an entirely new carcinoma of the cardia of the stomach with extension into the esophagus. In previous years, this patient would have been considered inoperable because of the esophageal extension. However, he was operated upon and a thoraco-abdominal total gastrectomy was done. The patient, seen this year, was completely recovered with no evidence of recurrence. He has been given at least three years, and possibly more, of healthful life by the second operation for a second gastric carcinoma. Our surgeons are not optimistic about "second-look" operations for cancer of the stomach, or operations for recurrent cancer. They try to be as radical as possible with the first operation. It is to be expected, therefore, that recurrences are usually nonresectable and noncurable. Six patients with recurrent carcinomas of the stomach who have been operated upon have not been appreciably helped by the second operation.

Summary

The surgical approach to the problem of gastric cancer in the years 1940 through 1945 has been reviewed and compared with the present surgical attack (1950 through 1951). This comparison demonstrates several changes:

1. Little is left to "clinical judgment" short of exploration.

2. Physical examination rarely determines operability. A fixed mass with apparent extension of the tumor may actually be a resectable lesion.

3. Operability is never determined by roentgen examination of the stomach. What may appear to be an inoperable carcinoma on such study may actually be a mesenchymal tumor or even severe hypertrophic gastritis.

4. Esophageal involvement is not a contraindication to surgery.

5. A tissue diagnosis is desirable in every case. A suspected carcinoma with metastases such as a supraclavicular node or a rib lesion may actually be a lymphoblastoma sensitive to roentgen therapy. A hard nodular liver may be a

cirrhotic liver, and a Blumer's shelf may be lipogranuloma, chronic inflammatory pelvic mass and in the female an incarcerated, retroverted uterus.

6. The operability and resectability rates have increased, possibly resulting in more potential cures, and we believe will increase the number of five year survivors.

7. Extension of the disease to neighboring organs and lymph nodes is not necessarily a contraindication to resection. Some of these patients, with adequate resections, have been five year survivors.

8. More total gastric resections and more complicated resections with removal of adjacent organs are being performed. This should result in a greater chance for five year survival in a greater number of patients.

References

1. Wangensteen, O. H.: Cancer of the esophagus and the stomach. The American Cancer Society, Inc., New York City, New York, 1951.

2. Guiss, L. W.: End results for gastric cancer; 2,891 cases. Surg., Gynec. & Obst., **93**:313-331 (Oct.) 1951.

3. Lahey, F. H. and Marshall, S. F.: Should total gastrectomy be employed in early carcinoma of stomach? Experience with 139 total gastrectomies. Ann. Surg. **132**:540-560 (Sept.) 1950.

4. Lahey, F. H.: Total gastrectomy for all patients with operable cancer of the stomach. Surg., Gynec. & Obst. **90**:246-248 (Feb.) 1950.

5. Longmire, W. P., Jr.: Total gastrectomy for carcinoma of stomach. Surg., Gynec. & Obst. **84**:21-30 (Jan.) 1947.

6. Pack, G. T. and McNeer, G.: Total gastrectomy for cancer; collective review of literature and original report of 20 cases. Internat. Abstr. Surg. **77**:265-299, 1943.

7. McNeer, G., VandenBerg, H., Jr., Donn, F. Y. and Bowden, L.: A critical evaluation of subtotal gastrectomy for the cure of cancer of the stomach. Ann. Surg. **134**:2-7, 1951.

8. Lahey, F. H.: Discussion. Gastroenterology. **22**:75-77 (Sept.) 1952.

9. McNeer, G., Booher, R. J. and Bowden, L.: Resectability of recurrent gastric carcinoma. Cancer **3**:43-55 (Jan.) 1950.

10. Brown, C. H. and Kane, C. F.: Carcinoma of the stomach: Review of 406 cases seen from 1940 to 1945: Operability, resectability and curability. Gastroenterology. **22**:64-75 (Sept.) 1952.

11. Maimon, S. N. and Palmer, W. L.: Gastric cancer: diagnosis, course, and prognosis. Postgrad. Med. **6**:201-211 (Sept.) 1949.

12. Pack, G. T.: The changing prognosis for cancer of the stomach. CA. **1**:112-117 (May) 1951.

13. Berkson, J., Walters, W., Gray, H. K. and Priestley, J. T.: Mortality and survival in cancer of the stomach: A statistical summary of the experience of the Mayo Clinic. Proc. Staff Meet. of the Mayo Clinic. **27**:137-151 (April 9) 1952.

THE ROENTGENOLOGIC DIAGNOSIS OF JEJUNAL OR MARGINAL ULCER

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PROMPTED by a desire to improve our accuracy in the roentgenologic diagnosis of marginal or jejunal ulceration, we reviewed all cases in which exploration had been carried out because of a provisional diagnosis of such ulceration. Fifty-six patients who had been operated upon within six months of roentgenologic examination are included in this series.

Of these 56 cases, a marginal or jejunal ulcer was found at surgery in 37 patients. Scarring at the site of anastomosis without evidence of ulcer was evident in two patients, a jejuno-gastro-colic fistula was found in four instances and a gastroileostomy in two. In 11 cases there was no evidence of ulceration.

In the 37 surgically proved ulcers a positive radiographic diagnosis had been made in 19. An equivocal diagnosis had been made in seven and a negative diagnosis in 11 cases. This corresponds to the findings of Priestley and Gibson[1] who report 52 per cent accuracy in the roentgenographic diagnoses of marginal ulcers.

Ulcers were presumed to have been present in both cases in which scarring was found at the site of anastomosis.

Correct diagnoses were made in three cases of gastro-jejuno-colic fistula prior to surgery, and in one case of gastroileostomy.

Of the 11 negative explorations, correct preoperative diagnoses were made in five, equivocal diagnoses in three, and positive or incorrect diagnoses in three cases.

Twenty-four patients with proved ulcer had had simple gastroenterostomies; in five, gastroenterostomies had been combined with vagotomies; seven had undergone subtotal gastric resections and, in one case, the original surgery was not recorded. For obvious reasons these figures do not indicate the relative incidence of ulceration following the various types of gastric surgery.

The average interval between radiographic diagnosis and final surgery was 28 days. The longest period was six months and the shortest, one day.

The average interval between the initial surgical procedure and final exploration was eight years. Thirty-one years was the longest period of time, and three months the shortest. Thus it is seen that ulceration developed within three months of the original surgery in one case in this series.
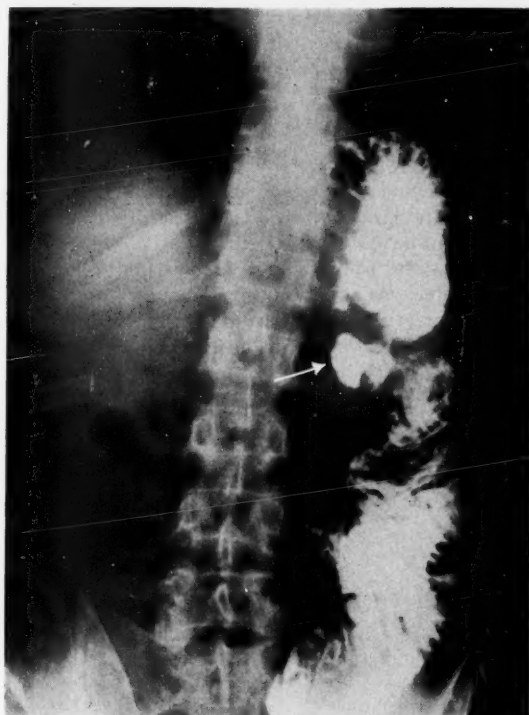
Fig. 1. (a) Subtotal gastrectomy and gastrojejunostomy with subsequent jejunal ulceration. The large collection of barium (at arrow) represents a walled perforation.

Thirty-two ulcers were found in men and five in women. While this of course does not necessarily indicate the relative incidence of ulceration in men and women, it is in agreement with the figures of Beck[2] who found that 12.5 per cent of marginal ulcers occur in women.

Review of Films

Upon consideration of the preceding figures it was felt that the accuracy of diagnosis might be improved if the films were reviewed. Reexamination of these films disclosed a great variation in ulcer size: surgical reports showed that they varied from 0.3 to 3.5 cm. in diameter. These reports did not differentiate simple ulcerations and those ulcerations which had perforated and subsequently walled off. Undoubtedly those which are several centimeters or more in depth

represent the latter condition. Radiographically these are seen as large collections of barium representing the extent of the walled off perforations. Several of these had been mistakenly diagnosed as "surgical pockets."

Although the actual size was not recorded in all cases, it is apparent from the films that the walled off perforations may reach 4 or 5 cm. in diameter (fig. 1a).

Those which represented simple ulceration usually showed smooth shallow crater formation, and the large walled off areas of perforation usually showed slight irregularity of outline. Most cases demonstrated large folds in the jejunum which appeared to radiate from the site of ulceration (fig. 2). In one case filling of the ulcer crater was apparently prevented by obstruction of the jejunum, presumably secondary to the ulceration (fig. 3). Eusterman and Kirklin[3] found that 77 per cent of patients with obstruction of the jejunum had associated ulceration.

From the surgical reports it was not possible to determine the exact location of the ulceration in all cases, but the majority of ulcers were located in the
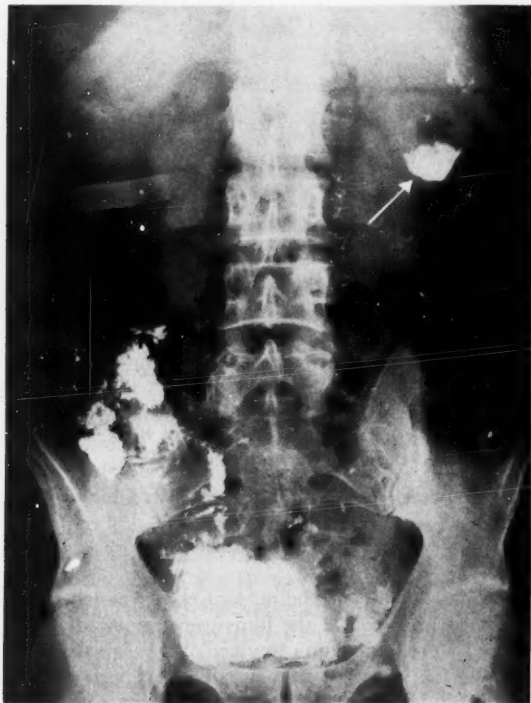
FIG. 1. (b) Six hour retention film demonstrating retention of barium in the large crater.

Fig. 2. Gastroenterostomy with subsequent jejunal ulceration demonstrating characteristic radiating mucosal folds.

jejunum several centimeters from the stoma. In only one instance was the ulcer actually "marginal," i.e., located at the stoma.

Of 13 of the 37 cases demonstrating marginal ulceration, retention films were made from 3 to 24 hours following the examination. In each of these, barium was retained in the crater (fig. 1b). In some patients, however, considerable barium was retained in the intestinal tract, obscuring detail so that accurate localization of the crater was not always possible.

Technic of Examination

As a result of this study a modified technic for the examination has been instituted for patients with suspected marginal ulceration.

The patient is first given one swallow of barium mixture under fluoroscopic control. Spot films of the stoma are made and, subsequently, anterior-posterior and posterior-anterior survey films. The entire cup of barium is then given.

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FIG. 3. Subtotal gastric resection with gastrojejunostomy. Arrow points to narrowed obstructed efferent limb of the jejunum. A large associated jejunal ulceration was found at surgery.

Spot films are taken in upright and horizontal positions. Following this, anterior-posterior, posterior-anterior, right anterior oblique and left posterior oblique films are made.

A four hour retention film is then taken and reviewed in conjunction with the preceding ones. If the diagnosis of ulceration is not confirmed or excluded, a repeat fluoroscopic examination is performed with particular attention to any suspicious, retained flecks of barium.

In the few patients we have had the opportunity to examine since institution of this technic, the accuracy of diagnosis appears to have been greatly improved, but a sufficient number of cases has not been accumulated to permit accurate evaluation.

Summary

1. A series of 56 patients explored for jejunal ulcer has been reviewed.

2. Review of the films has demonstrated that marginal ulcerations with subsequent perforation may reach the unusually large size of 4 or 5 cm. in diameter.

3. Characteristic radiating folds of jejunal mucosa frequently occur about the area of ulceration.

4. Every retention film made demonstrated retained barium in the ulcer crater.

5. A technic is described which we believe will improve the accuracy of roentgenologic diagnosis of marginal or jejunal ulceration.

References

1. Priestley, J. T. and Gibson, R. H.: Gastrojejunal ulcer: clinical features and late results. Arch. Surg. 56:625-641, 1948.

2. Beck, W. and Watson, J.: Gastrojejunal ulcer. Guthrie Clin. Bull. 17:105-111 (Jan.) 1948.

3. Eusterman, G. B., Kirklin, B. R. and Morlock, C. G.: The nonfunctioning gastroenteric stoma: diagnostic study of sixty-two surgically demonstrated cases. Am. J. Digest. Dis. 9:313-317 (Oct.) 1942.

4. Mayo, Henry, Jr.: The physiologic basis of operation for duodenal gastric and gastrojejunal ulcer. Surgery 26:251-330 (Aug.) 1949.

RESISTANT CASES OF MENIERE'S DISEASE*

Treatment by Labyrinthotomy

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M UCH has been written about Meniere's disease and its treatment since Meniere's initial classic description in 1861. Many theories and explanations have been offered in an attempt to clarify the problems involved. This fact alone signifies that a certain amount of confusion, with regard to the etiology and pathology as well as the treatment of the disease, has existed. It has mainly been in the past decade that writers such as Day[1] have clarified the meaning of the term "Meniere's disease," and differentiated between it and the pseudo-Meniere's disease, which Dandy used to label those cases which had only vestibular involvement.

The term Meniere's disease is reserved for that group of patients presenting the syndrome comprising vertigo, tinnitus, deafness and sometimes nausea and vomiting, for which no definite systemic or local condition can be blamed. Heretofore, many patients with dizziness and nausea or vomiting were diagnosed as having Meniere's disease even though there was no cochlear involvement. Meniere's syndrome, or components, may be caused by a variety of conditions but now, it is generally agreed, only the patients belonging to the idiopathic group warrant a diagnosis of Meniere's disease.

Etiology

Investigators have attempted to prove the etiology of Meniere's disease for many years. Meniere's syndrome may have toxic origin such as poisoning from lead, arsenic in alcohol, mercury, salicylates, and other drugs. It is also present with chronic infections, the exanthemata, syphilis, tuberculosis, the anemias, leukemias, virus infections, purpuras, tumors of the cerebellopontine angle, trauma, and gastrointestinal conditions.[2] Among the simple local causes are impacted cerumen and blockage of the eustachian tube. The syndrome may be present in catarrhal or suppurative otitis media, vasospasm, hemorrhage or thrombosis of labyrinthine blood vessels, arteriosclerosis of cerebral vessels,

neoplasms, labyrinthitis, multiple sclerosis and other degenerative central nervous system diseases.[3] Some cases have been reported on the basis of allergy. Diet is thought to be a factor by some investigators. The basis of Meniere's syndrome or symptom complex may be summarized as vascular, inflammatory, degenerative or neoplastic lesion, which may be peripheral or central.

In 1938 Cairns and Hallpike[4] gave a historic paper on the histopathology in Meniere's disease. They reported on sections of the temporal bones of three patients who had been previously operated upon for Meniere's disease by sectioning of the eighth cranial nerve. Their findings consisted of a dilated endolymphatic system, degeneration of the organ of Corti and stria vascularis and a pathologic elevation of the otolithic membrane of the utricle. The basic pathology appears to be the dilatation of the cochlear duct which encroached on the utricle and saccule. They postulated that the crisis in the disease did not occur until dilatation of the membranous canal was completed to the full extent of the bony canal. After this was accomplished, any further increase in pressure of the endolymph precipitated a crisis. It has since become accepted by many investigators that hydrops of the labyrinth is the pathologic change peculiar to Meniere's disease.

However, postulation continued regarding the endolymph,[5] the decreased resorption of it, or possible chemical changes in the endolymph and perilymph. This point has not been proved. One theory is that a disturbed sodium metabolism with retention of sodium ions is the underlying causative factor. Another is that it is a vascular disturbance, probably a vasoconstriction. Williams[6] feels it is basically an inherent allergic problem. Lindsay's[5] work with monkeys showed that the volume of endolymph did not depend upon a functioning ductus endolymphaticus or even upon its existence. He also demonstrated that the hydrops of Meniere's disease could not be attributed to interference of absorption of endolymph from its dilated and convoluted middle portion.

Symptomatology

Meniere accurately described the symptoms of the disease that bears his name. The symptoms of tinnitus, deafness, vertigo, nausea and vomiting without neoplastic, vascular, or inflammatory cause associated, are the basis of the diagnosis. The disease occurs in episodes or attacks which are characteristically remittent. The symptoms may completely or only partially disappear between attacks.

The vertigo may take various forms. It is vertigo in its most accurate sense if the patient experiences a sense of motion, rotary or linear, and a disorientation in space. It may be objective, in which case the surroundings seem to move; or subjective, in which circumstance the individual feels as if he were moving. This may also take the form of tactile error in which the floor seems to tilt, or roll like the deck of a ship at sea. The vertigo may be of sufficient severity to cause staggering or even falling. Motion of the head aggravates this condition and so the patient tends to remain quiet and to assume the most comfortable position.

The deafness may be of varying degrees, but usually involves the entire scale. There is decreased bone conduction and the audiogram shows a "nerve deafness" curve. Diplacusis and distortion occur and may be annoying symptoms. It has been noted and emphasized that cochlear involvement is bilateral[7] which may help to explain the distortion. It is also believed that the sound is carried or referred farther down the basilar membrane than is normal for its pitch, as a result of the increased pressure in the endolymph. The diplacusis and distortion tend to disappear as the deafness becomes more critical.

The tinnitus usually has two components which vary in intensity: One is a high-pitched hissing, ringing, or whistling; the other is a low-pitched roaring or throbbing and may be synchronized with the heartbeat. The latter is often the more troublesome and annoying.

Nausea and vomiting are not always present. These two symptoms indicate acuity and severity and may necessitate hospitalization for parenteral feeding to prevent prostration in extreme cases.

The symptoms at the time of onset are unilateral in approximately 90 per cent and bilateral in about 10 per cent of the cases.[5] However, evidence of bilateral cochlear involvement has been shown in as many as 86 per cent of a series.[7] Other authors state that bilateral involvement is more frequent than formerly presumed. There are varying degrees of the disease. Early in the course there may be symptoms of involvement of either the vestibule or cochlea, but eventually both are affected.

Caloric tests for vestibular function show a nonfunctioning or hypoactive labyrinth on the affected side. The supposedly unaffected side may show a similar diminution in response. Usually the more severe the deafness, the less the caloric response. The caloric response will simulate the spontaneous attacks.

Diagnosis

In arriving at a diagnosis one must take a careful history, do a thorough ear, nose and throat examination and eliminate general or systemic causes of the symptoms. The history is of such great importance that a diagnosis can almost be made from it alone. It is essential to discern the type of dizziness, whether subjective or objective, and distinguish between vertigo and a mere giddy or lightheaded sensation. Other salient points are to be considered such as: Is it associated with tinnitus, deafness, nausea or vomiting? Does it occur in attacks, or is it constant? Cochlear involvement must be present to make a diagnosis of true Meniere's disease.

Inasmuch as many general or systemic conditions or lesions outside the labyrinth can cause certain symptoms of Meniere's syndrome, it is necessary to exclude them by history, physical examination and the aid of the laboratory. A complete ear, nose and throat examination is done to eliminate any apparent local cause. Such examination may disclose blocked eustachian tubes, cerumen

impaction or local inflammation. Conversely, there may be no obvious cause for the symptoms and the physical examination will reveal nothing abnormal except a nerve deafness curve on the audiogram and diminished caloric response of the labyrinth. Spontaneous nystagmus of the rotary type is also an important indication of labyrinthine involvement but it is not always present. It is usually experienced during or shortly after an attack. The possibility of an acoustic neurinoma or other intracranial lesions should not be overlooked.

Having precluded inflammatory, vascular, neoplastic and general systemic causes; having localized the lesion to the vestibule with cochlear involvement; and having confirmed the syndrome of vertigo, tinnitus, and deafness with possible nausea and vomiting, one may arrive at a diagnosis of Meniere's disease.

Medical Treatment

Once the diagnosis is established, medical treatment should be the first alternative. This form of management affords definite improvement or controls the vertigo in 85 per cent, improves or relieves tinnitus in 50 per cent and improves hearing to some extent in 20 per cent.[8] The estimates and affirmations vary depending upon author and treatment employed, but the foregoing figures are a general average.

The various forms of medical treatment depend upon the accepted etiology. One theory is that Meniere's disease is due to water imbalance with retention of fluid; thus, the therapy is limitation of fluid intake to induce dehydration. Another is that electrolyte imbalance is the causative factor and potassium is given as treatment. Still other investigators claim good results by nicotinic acid administered to relieve vasoconstriction.[9] One of us first reported the beneficial effects of nicotinic acid in March 1940.

In our experience the nicotinic acid regimen and a hypo-allergic diet have brought favorable results in between 80 and 90 per cent of the cases treated. Occasionally, dramamine has been added when the patient did not respond satisfactorily; this has proved valuable in some of the more resistant cases. Other patients may obtain benefit from a mild sedative added to the regimen.

Surgical Treatment

There are two sites of surgical attack for operative treatment. One is the acoustic nerve, which is partially or completely sectioned, and the other is the end organ in the inner ear which is destroyed by various means. Both have their proponents. More recently a third site, the autonomic nervous system, has been interrupted, based on the belief that the etiology of Meniere's disease is vasoconstriction.

Ray[10] and others have used the intracranial sectioning of the acoustic nerve, either partial or complete. The partial sectioning was done on the anterior one-half to five-eighths of the nerve in an attempt to interrupt the vesti-

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bular fibers and preserve the cochlear fibers and the hearing.[11] Better results in relief of the vertigo are obtained by complete sectioning of the nerve as no vestibular fibers are missed. The vertigo has been relieved or improved in 95 to 100 per cent of these patients[8] and the tinnitus has been partially relieved or improved more decidedly by total section than by partial section of the nerve. Hearing has been preserved in some with partial section, but these patients are also more likely to have some persistent vertigo and tinnitus. The hearing is usually not serviceable in these patients who are selected for surgical treatment; consequently little is gained by preserving it.

A number of operations on the end organ have been performed with varying results. It was hoped that a means of relieving the vertigo and tinnitus could be devised at this site and still preserve the hearing. In England investigators[12,13,14] injected alcohol through the oval window or a trephine in the lateral semicircular canal into the labyrinth after a mastoid approach was effected. This always destroys hearing but frequently results in a facial paralysis. The drainage of the saccus endolymphaticus affords only temporary relief and others have not had as much success with this procedure as Portmann who introduced it. Experiments with monkeys[5] showed that the drainage and destruction of the saccus endolymphaticus was followed by sealing and healing without effect on the labyrinth beyond; and, therefore, could only give temporary relief of vertigo though it preserved hearing.

It has also been demonstrated that ablation or avulsion of the membranous semicircular canal destroys the function of the canal but has no effect on hearing if the ampullary end remains intact. Cawthorne removed the membranous canal and ampulla, and though the vertigo was cured, hearing was lost.

One operator used the intracranial route to apply a coagulating current within the superior semicircular canal in an attempt to destroy the vestibule and preserve the cochlea. Day[1,3] admitted this method was plausible, but not the best approach. Subsequently, he devised the following method: Through a partial, simple mastoidectomy by the postauricular route, he opened the horizontal semicircular canal near the ampulla and inserted a coagulating needle into the vestibule. A light coagulating current was applied two or three times for about one second each. He was successful in relieving vertigo with little postoperative morbidity or risk to the patient. At first he reported the effect on hearing varied from complete loss to return to normal. More recently he and others report loss of hearing as the more frequent result. The low-pitched tinnitus is usually relieved; the high-pitched type persists but it is not often a serious complaint.

The success of this procedure led to further investigation as to its effect on the end organ and the possibility of controlling the current so as to preserve the cochlea and destroy only the vestibule. Experiments on rabbit ears treated by coagulation and trauma showed pathologic change in the vestibule but none in the auditory apparatus. Thus, the cause of deafness following the coagulation procedure was unexplained. Simple decompression of the perilymph was also shown to be valueless.[5]

Schlander[15] reported that it is not the coagulating effect of the current that destroys the labyrinth, but that hemorrhage into the perilymphatic space at the time of surgery is followed by a serofibrinous labyrinthitis which destroys the inner ear. Schall and Rambo,[16] working with monkeys, concluded that where optimum current is used, the damage to the vestibular mechanism is unpredictable and that retention of serviceable hearing is improbable. The facial nerve was not damaged in any of these animals. Lempert[17] states that tinnitus and vertigo should both be relieved by aseptic decompression of the cochlea and vestibule. He reported success in relieving tinnitus in nine of ten, and vertigo in all ten cases by opening the oval and round windows.

Passe and Seymour[2] reported on a series of operations in which the autonomic nervous system was interrupted. They pointed out that the blood supply to the inner ear is from the internal auditory artery, from the anterior inferior cerebellar artery, or from the basilar artery which is formed by the union of the vertebral arteries. After the internal auditory artery goes through the internal auditory meatus it divides into the cochlear and vestibular arteries which may be equal or unequal in size. The variability of distribution could account for the predominance of vestibular or cochlear symptoms in some cases by accepting the vasoconstriction theory as the cause of Meniere's disease. Also a smaller sized vessel could have greater vasoconstrictive power by virtue of its size.

Since, it has been shown that vasoconstrictor fibers are exclusively sympathetic ganglionic; that there are intramural fibers in some vessels, and that vasospasm recurs after periarterial sympathectomy; it was considered necessary to destroy the cell station in the stellate ganglion and to strip and cut the vertebral artery to interrupt all vasoconstrictor impulses. A neck approach was used; the vertebral artery was cut and ligated; the stellate ganglion was excised, and the preganglionic fibers of T1 and T2 were cut.

These patients develop a Horner's syndrome immediately which gradually improves over a period of months. The authors claim relief of vertigo and improved hearing with varied effects on tinnitus. Arteriosclerotic patients are never subjected to this operation because of the danger of thrombosis of the posterior inferior cerebellar artery; nor is the operation ever performed bilaterally. This is a radical procedure and further investigation is necessary to prove its worth.

Selection of Cases

Every case presenting the symptoms of Meniere's disease should be observed for a sufficient period of time to confirm the diagnosis of Meniere's disease according to the criteria mentioned previously in this paper. Medical treatment should then be given an adequate trial as it will control about 80 to 90 per cent, and the disease characteristically goes through remissions which may last for many months or years.

If medical treatment fails after a four to six months' period, surgical relief

should be advised. Before deciding to operate upon these patients, one must carefully determine the presence and extent of general systemic diseases which might offer a contraindication to surgery. Life expectancy should be such that the procedure is practicable. The economic position of the patient is also a factor in determining the extent of his incapacity. If he has a hazardous occupation or cannot afford to stay away from work and spend time and money for prolonged medical treatment, he should have the operation. The amount of hearing loss is also a factor in deciding upon surgery, as the procedures which relieve vertigo with the best results also destroy hearing. Therefore, we feel that hearing should be below the serviceable level on the side to be operated upon. Furthermore, the operation should be performed on one side only as those who have the vestibular function destroyed bilaterally do not compensate for this loss. The symptoms are usually due to the disease in one ear and operation gives relief. If the other ear causes symptoms, the attacks are well controlled by medical management as a rule, especially if treatment is started when the symptoms originate.

While there are valid points in favor of each of the various procedures, we feel that the labyrinthotomy with electrocoagulation of the labyrinth is the treatment of choice in the proved cases resistant to medical management. Our reasons for this conclusion are that the results are excellent for relief of vertigo, the procedure is relatively short, requiring about 30 minutes, is fairly simple, and the risk to the patient is minimal; a craniotomy is avoided. This method attacks the site of pathologic change in the labyrinth, and is therefore logical. It requires only a short period of hospitalization of five to seven days, recovery is rapid, and no facial paralysis has occurred in our cases.

Summary

The vertigo was relieved in all these 12 patients observed by us and the hearing, which was below the serviceable level in the ear operated upon, was further diminished by the procedure. The effect on the tinnitus was variable, but for the most part the condition was not improved. These patients were definitely benefited and rehabilitated economically. Each case is considered as having been successful. No facial paralysis occurred; there was no postoperative infection, and healing was rapid. Antibiotics were used. The hospital stay averaged six days.

The etiology, symptomatology and diagnosis of Meniere's disease were reviewed. It is emphasized that medical treatment gives good results in the vast majority of cases and should be given a thorough trial before surgical treatment is considered. The various surgical procedures are discussed with emphasis on labyrinthotomy and destruction of the membranous labyrinth by electrocoagulation. Factors in selection of patients for surgical treatment are reviewed and reasons advanced for choosing this procedure in 12 cases treated over the past two and a half years.

Conclusions

1. Patients with Meniere's disease who cannot be controlled by medical treatment should have the benefit of surgery.

2. Labyrinthotomy and destruction of the membranous labyrinth has proved effective in the control of vertigo of labyrinthine origin.

3. The procedure should be reserved only for the few carefully selected patients that defy good medical management and who have hearing in the involved ear that is below the serviceable level.

4. This is not the final answer to this problem even though the patients are rehabilitated economically, since hearing is not restored to normal.

5. A plea is made for the early diagnosis and recognition of the true nature of this disease, as vasodilators such as nicotinic acid (especially when given early) will nearly always control the symptoms and prevent or delay its progress, thus preserving hearing at serviceable levels.

References

1. Day, K. M.: Surgery of labyrinth for Meniere's disease. Tr. Am. Acad. Ophth. (1943) **48**: 221-230 (March-April) 1944.

2. Passe, E. R. G. and Seymour, J. S.: Meniere's syndrome; successful treatment by surgery on the sympathetic. Brit. M.J. **2**: 812-816 (Nov. 6) 1948.

3. Day, K. M.: Diagnosis and surgical treatment of Meniere's disease (hydrops of labyrinth). Ann. Int. Med. **23**: 41-47 (July) 1945.

4. Cairns, H. and Hallpike, C. S.: Meniere's syndrome. Lancet **1**: 1163-1165 (May 21) 1938.

5. Lindsay, J. R.: Labyrinthine surgery for Meniere's disease. Tr. Am. Acad. Ophth. **53**:527-537 (May-June) 1949.

6. Williams, H. L.: Indications for surgical treatment in Meniere's disease. S. Clin. North America **29**:1077-1091 (Aug.) 1949.

7. Cawthorne, T. E., Fitzgerald, G. and Hallpike, C. S.: Studies in human vestibular function; observations on clinical features of "Meniere's" disease, with especial reference to results of caloric tests. Brain **65**:161-180 (June) 1942.

8. Talbott, J. H. and Brown, M. R.: Meniere's syndrome; acid-base constituents of blood; treatment with potassium chloride. J.A.M.A. **114**:125-130 (Jan. 13) 1940.

9. Harris, H. E. and Moore, P. M., Jr.: Use of nicotinic acid and thiamin chloride in treatment of Meniere's syndrome. M. Clin. North America **24**:533-542 (March) 1940.

10. Ray, B. S.: Meniere's disease; its surgical treatment by division of acoustic nerve. Am. J. Surg. **75**:159-170 (Jan.) 1948.

11. Walsh, M. N. and Adson, A. W.: Meniere's syndrome; medical vs. surgical treatment. J.A.M.A. **114**:130-135 (Jan. 13) 1940.

12. Yearsley, M.: Operative treatment of labyrinthine vertigo. Lancet **2**:618-619 (Sept. 10) 1938.

13. Wright, A. J.: Vertigo treated by destruction of labyrinth. Lancet **1**:1165-1166 (May 21) 1938.

14. Yearsley, M.: Further case of labyrinthectomy. Lancet 1:548-549 (March 23) 1940.

15. Schlander, E.: Tierexperimentelle Untersuchungen des Labyrinths nach der Day'schen Operation. Acta oto-laryng. (1948) supp. **78**:119-129, 1949.

16. Schall, L. A. and Rambo, J. H. T.: Electrocoagulation of membranous labyrinth; experimental histological studies in monkey. Ann. Otol., Rhin. & Laryng. **57**:590-602 (Sept.) 1948.

17. Lempert, J.: Lempert decompression operation for hydrops of endolymphatic labyrinth in Meniere's disease. Arch. Otolaryng. **47**:551-570 (May) 1948.

18. Altmann, F.: Surgical treatment of Meniere's disease. Laryngoscope **59**:1045-1067 (Oct.) 1949.

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ST. LUKE, THE PHYSICIAN

A. C. CORCORAN, M.D.
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That,

> "Matthew, Mark, Luke and John
> Went to bed with their britches on,"

epitomizes in a jingle from childhood all that most of us know of the lives and habits of the four Evangelists. Indeed, one measure of their greatness is that they did not intrude themselves into their books. Still, writers who are so widely read and whose influence is so momentous should not remain to us more as names than as men. Unfortunately, time and the greater significance of their messages obscure the record. Across the 2000 years we have to inform us only "faint clues and vague indirections."

The life of St. Luke, author of the Third Gospel and of the Acts of the Apostles, is of particular interest to physicians, because he was one of us. His feast day is October 18; he is appropriately remembered at this later date because most that we associate with the Christmas season is of his telling; he describes the Annunciation by the Angel, Mary's hymn of praise, the Magnificat, her visit to Elizabeth, the scene at Bethlehem and the story of the shepherds watching their flocks by night. Perhaps because he could paint so well in words, tradition has it that he used colors too; at least, his graphic descriptions have inspired many centuries of Christian art.

Any approach to telling the story of his life requires some guessing and a measure of presumption. First, to place him in his setting: the Roman Empire had spread over all the shores of the Mediterranean; with the freedoms of many other peoples, Rome had captured those of disunited Greece. Horace expressed the general feeling of Roman intellectuals when he acknowledged that, "Conquered Greece still had the Victory"; the Greeks acknowledged Roman law, but retained their positions as teachers, traders and professional men on all the shores of the Inland Sea. Everyone, Greek and Cypriot, Roman and Jew, Syrian and Phoenician, had a common bond of Hellenistic culture.

The Roman Peace spread in ever widening circles; but the prosperity and commerce and opportunities for leisure brought stability and order in only a superficial sense. The souls of the people were restless. Many recognized that the gods of Olympus were dying or dead, so that polytheism persisted as more of a social than a religious system. The idea of one God was renewed time after time by cults which arose at the eastern borders of the Empire, usually at the edges of the deserts. These in their various forms, some of them hideous, gained eager candidates. Even a nationalistic and nonproselyting Judaism had almost grudgingly to accept many pious Gentiles; these, like the youthful St. Luke

and the "centurion in Caesarea called Cornelius" entered the company of those who "feared God" by accepting decalogue and synagogue.

St. Luke's family were Greeks of Antioch in Syria, where probably he was born (c. 17 B.C.). His name (Lukas) is the Hellenized form of the common Roman name, Lucanus, and it may have been that his father was the freed slave of a Roman family. Slavery did not then imply the mental degradation which it does now, and it is likely that his education and that of his family were exceedingly advanced. In any case, it was an education for a bright boy merely to live in the currents of trade and opinion that flowed from Arabia and Persia to Gaul and farthest Britain.

Part of his education may have been rabbinical; at least, he was profoundly versed in the Law and the Prophets. He was also well trained in Greek, and St. Jerome considered him the "most learned in the Greek tongue of all the evangelists." As a result, his style can be "as Hebraistic as the Septuagint and as free from Hebraisms as Plutarch." He is Biblical when he treats of the Law or records the songs of Simeon and of Mary; when free to report events which have no specific connotations, he does so in straightforward and erudite Greek, avoiding and correcting the flaws of grammar and phrasing of the earlier Gospel of St. Mark. In fact his style is that of the written word, while the other Gospels have the character of speech and declamation; this is because the other Evangelists were not lettered men, but preachers.

He probably obtained his medical education in Tarsus, a school which at that time rivaled those of Alexandria and of Athens. It may have been there that he first met Saul, later Paul, at that time filled with fervor from the knees of Gamaliel at Jerusalem. They had at least the opportunity to meet, for Saul, a native of the town, was a Roman citizen by birth while Luke attained that dignity with his profession. In any case, tradition goes on to relate that Luke first practiced at Antioch. He tells us that it was here that the disciples were "first called Christians." Here, perhaps for the second time, he fell under the spell of the convert Paul, joined him, and after a delay which may have allowed the disposal of his practice, set out in the fall of the year 50 to meet St. Paul at Troas.

There, from the site of ancient Troy whence Ulysses and Aeneas had sailed a thousand years before, began St. Luke's journeys as "the beloved physician." At this point in Acts, the account changes from an impersonal recital (pronoun, "they") to the diary form of a companion and eyewitness (pronoun, "we"): "straightway we sought to go forth into Macedonia." First they went to Phillipi, "the chief city of that part of Macedonia and a (Roman) colony," where St. Luke stayed while St. Paul went on to preach at the altar of the Unknown God in Athens and to Corinth and Ephesus. Meanwhile, a feeling had grown against St. Paul in the Palestinian Church, where many of the new Christians regarded his mission to the Gentiles and their conversions with jealousy. St. Paul decided to go to Jerusalem where this feeling was most intense. He disregarded warnings of persecution and set sail with St. Luke in their first long journey together.

St. Luke's next long journey began with St. Paul's imprisonment, his trials and the attempt at torture which resulted in the appeal to Caesar. They set out for Rome under guard and were shipwrecked at Malta on the way. His account ends about two years after their arrival in Rome, where St. Paul was still awaiting his trial. It may have been there that he wrote his books, "the Gospel as he had heard it, the Acts of the Apostles as he had witnessed it." (St. Jerome) St. Paul was condemned and executed some three miles from Rome at a place on the Ostian Way called Tres Tabernae. Only a little while before he wrote from prison that "only Luke is with me." From this time on, St. Luke's career is obscure. Tradition has it that he died at the age of 84 in Bithynia on the Asiatic shore of the Black Sea. St. Jerome states that his bones, with those of the apostle Andrew, were buried in Constantinople.

Thus, tenuously pieced, is the record of his life. More is revealed by indirection in his writings. The length of a book was then limited by the convenient dimensions of a manuscript roll. His two books are therefore brief, even though they contain more than one third of the New Testament. The canonical arrangement interposes the Gospel of St. John between books intended as volumes in a single work which were intended "to contain all things from the very first" in order to confirm the reader in "the certainty of those things wherein thou hast been instructed." "The first four verses of the Third Gospel of 42 words in the Greek (82 in English) exhibit more competency as witness and greater accuracy and convictions as to the truth of what he is about to write than, as far as I can discover, any equal number of words ever written, and that without the slightest apparent effort." (Dr. Howard Kelly) The books are clearly intended for general use, so that Theophilus, to whom they are dedicated, was probably not a person but a pun (Theophilus meaning lover of God). The abrupt ending with St. Paul still "preaching the kingdom of God and teaching those things which concern the Lord Jesus Christ, with all confidence, no man forbidding him" suggests that a third volume was projected. It is unlikely that it was written and lost; perhaps St. Luke's Grecian sense of the fitness of things was so outraged by the fatal judgment of Nero's court in the case of his friend and patient, that he had not the heart to continue the record.

The books show more than erudition and an ability to carry over into Greek the imagery and mannerisms of Semites. The fact that most Greeks thought anyone else a barbarian, emphasizes St. Luke's uncanny empathy. The story of the Good Samaritan, which he is the only one to tell, characterizes his spirit and is in keeping with the highest traditions of our profession. "But . . . (a certain lawyer) . . . said unto Jesus, and who is my neighbor? and Jesus answering said, A certain man went down from Jerusalem to Jericho and fell among thieves . . . (who) . . . wounded him and departed, leaving him half dead." Some passed him by, but the Samaritan, himself an outcast, had compassion and "went to him and bound up his wounds, pouring in oil and wine and . . . took care of him." Incidentally, the passage indicates St. Luke's profession; the lay custom was to pour oil in wounds, but its use with wine was medical.

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That St. Luke was a physician and that he even existed, was questioned and denied in the tide of the 19 century skepticism which began by rejecting tradition and ended in accepting much that was more fantastic and less credible. Someone recently managed to analyze St. Luke's works over several hundred pages without any noteworthy reference to its medical character. Such viewpoints are easily challenged for, tradition apart, St. Paul called him "the beloved physician." The other evidences are many and cumulative and only a few examples can be given here. Thus St. Mark, who was one of St. Luke's sources, says, "and a certain woman which had an issue of blood twelve years, and *had suffered many things* of many physicians, and had spent all that she had, and was *nothing bettered*, but rather grew worse"; St. Luke's revision reads "and a woman having an issue of blood twelve years, which had spent all her living upon physicians, neither *could she be healed of any*"; he thus corrects a slur on a profession too often blamed for not doing that which no one can do. St. Luke is medically specific in his descriptions of illness: St. Mark tells of a man with a withered hand, while St. Luke says it was the right hand; St. Mark tells of a man with an unclean spirit who came out of the tombs, and St. Luke characterizes the insanity by noting that "he . . . had for a long time worn no clothes, neither abode in any house." Then there is the brief but thorough description of the case of Publius' father in Malta who "lay sick of a fever and of a bloody flux." What may be a clinching argument is the occasional use of medical words in a nonmedical sense; for example, when he tells of the strengthening of the ship during the storm, he uses a word which means splinting, as in surgery.

Thus, St. Luke was a devoted man and a learned man and a physician who, although he left his profession, never forsook it. St. Jerome says that "Luke the physician by leaving to the Churches his Gospel and the Acts of the Apostles, has shown us how the Apostles became from fishers of fish, fishers of man; for he himself became from a physician of the body, a physician of the soul . . . and as often as his Book is read in the Church, so often does his medicine flow out." His Gospel, according to Renan, is "the most beautiful book ever written." Because he wrote with the mind and ordered manner of a scientifically trained intellectual Greek, his writings had the greatest possible influence on his contemporaries, and they have continued to wield this influence through successive generations. In part this reflects the noble spirit and high medical character of their author. The Mass of his feast has the appropriate phrase: "To me, O God, how wonderful are thy friends! Their power is exceedingly strong!"

RECENT PUBLICATIONS BY MEMBERS OF THE STAFF

Brown, C. H., Fisher, E. R. and Hazard, J. B.: Relation between benign ulcer and carcinoma of stomach; report of eight cases of malignant transformation. Gastroenterology **22**:103 (Sept.) 1952.

Brown, C. H. and Hoerr, S. O.: Treatment of duodenal ulcer. Postgrad. Med. **12**:308 (Oct.) 1952.

Brown, C. H. and Kane, C. F.: Carcinoma of stomach; review of 406 cases seen from 1940 to 1945. Gastroenterology **22**:64 (Sept.) 1952.

Caccamise, W. C. and Whitman, J. F.: Pulseless disease; preliminary case report. Am. Heart J. **44**:629 (Oct.) 1952.

Cole, H. N., Jr., Irving, R. C., Lund, H. Z., Mercer, R. D. and Schneider, R. W.: Gargoylism with cutaneous manifestations. A.M.A. Arch. Derm. & Syph. **66**:371 (Sept.) 1952.

Corcoran, A. C., Taylor, R. D. and Page, I. H.: Management of essential hypertension: Evaluation of its present status. Bull. Acad. Med., Cleveland **37**:15 (Oct.) 1952.

Crile, George, Jr.: Analysis of vagotomy controversy. Ann. Surg. **136**:752 (Oct.) 1952.

Crile, George, Jr.: Thyroiditis. Ann. Int. Med. **37**:519 (Sept.) 1952.

Crile, George, Jr.: Treatment of chronic ulcerative colitis. Kansas City Med. J. **28**:9 (Nov.-Dec.) 1952.

Crile, George, Jr.: Treatment of intractable ulcerative colitis. Postgrad. Med. **12**:339 (Oct.) 1952.

Crile, George, Jr., Hoerr, S. O. and Collins, E. N.: Comment. Vagotomy problem. Gastro-enterology **21**:591 (Aug.) 1952.

Dempsey, W. S., Crile, George, Jr. and Engel, W. J.: Hypernephroma with metastasis to thyroid gland. J. Urol. **68**:576 (Sept.) 1952.

Dinsmore, R. S.: Foreword. Cleveland Clinic Issue, Postgrad. Med. **12**:287 (Oct.) 1952.

Dismore, R. S.: Changing status of hyperthyroidism. Univ. Michigan Med. Bull. **18**:255 (Sept.) 1952.

Effler, D. B.: Hiatus hernia. Postgrad. Med. **12**:317 (Oct.) 1952.

Ernstene, A. C.: Complications and sequelae of acute myocardial infarction. J.A.M.A. **150**: 1069 (Nov. 15) 1952.

Haserick, J. R. and Long, Roland: Systemic lupus erythematosus by false positive serologic tests for syphilis; presentation of five cases. Ann. Int. Med. **37**:559 (Sept.) 1952.

Hazard, J. B. and Kaufman, N.: Survey of thyroid glands obtained at autopsy in so-called goiter area. Am. J. Clin. Path. **22**:860 (Sept.) 1952.

Higgins, C. C.: Cystectomy for carcinoma of bladder: review of 68 cases. Ninth Congress Internat. Soc. Urol. **1**:129 (Sept. 15-18) 1952.

Higgins, C. C.: Management of patients with renal lithiasis. Postgrad. Med. **12**:345 (Oct.) 1952.

Hoerr, S. O.: Diseases of gallbladder and biliary tract. Postgrad. Med. **12**:353 (Oct.) 1952.

Hoerr, S. O., Brown, C. H., Rumsey, E. W. and Crile, George, Jr.: Duodenal ulcer. J.A.M.A. **149**:1437 (Aug. 16) 1952.

Humphrey, D. C.: Chronic pyelonephritis: an important cause of hypertension. Postgrad. Med. **12**:288 (Oct.) 1952.

Kolff, W. J. and Fisher, E. R.: Pathologic change after bilateral nephrectomy in dogs and rats. Lab. Investigation **1**:351 (Fall) 1952.

Krieger, J. S., Fisher, E. R. and Richards, M. R.: Multiple mesothelial cysts of peritoneum. Am. J. Surg. **84**:328 (Sept.) 1952.

McCubbin, J. W. and Page, I. H.: Influence of carotid sinus and aortic buffer reflexes and tetraethylammonium chloride on vascular reactivity to angiotonin and renin. Am. J. Physiol. **170**:309 (Aug.) 1952.

McCullagh, E. P.: Radioactive iodine in treatment of hyperthyroidism. **Ann. Int. Med.** **37**:739 (Oct.) 1952.

McCullagh, E. P.: Remarks on diabetic diets. **Bull. Acad. Med.**, Cleveland **37**:14 (Nov.) 1952.

Mercer, R. D.: Subdural hematoma in infancy. **Postgrad. Med. 12**:323 (Oct.) 1952.

Mullen, W. H., Jr. and Engel, W. J.: Circumcaval ureter. **Radiology 59**:528-537 (Oct.) 1952.

Page, I. H. and Corcoran, A. C.: Dietary treatment of hypertension. **J. Clin. Nutrition 1**:7 (Sept.-Oct.) 1952.

Page, I. H. and Brown, H. B.: Induced hypercholesterolemia and atherogenesis. **Circulation 6**:681 (Nov.) 1952.

Poutasse, E. F. and Fisher, E. R.: Amyloid tumor of urinary bladder. **J.A.M.A. 150**:96 (Sept. 13) 1952.

Poutasse, E. F. and McCullagh, E. P.: Cushing's syndrome. **J. Urol. 68**:779 (Nov.) 1952.

Schneider, R. W.: Diagnosis and treatment of hyperparathyroidism. **Postgrad. Med. 12**:293 (Oct.) 1952.

Schobinger von Schowingen, Robert: Further experiences in treatment of filariasis with hetrazan. **Acta Tropica 9** (No. 3) 1952.

Taylor, R. D. and Page, I. H.: On origin and properties of cerebral pressor substance (CPS). **Am. J. Physiol. 170**:321 (Aug.) 1952.

Turnbull, R. B., Jr. and Fisher, E. R.: Carcinoma in rectal polyp; follow-up observations on 27 patients. **Postgrad. Med. 12**:303 (Oct.) 1952.

Westcott, R. N.: Physiology of ventilation in chronic lung disease. **Postgrad. Med. 12**:329 (Oct.) 1952.

Williams, G. H., Jr., Karnosh, L. J. and Tucker, H. J.: Modification of signs in multiple sclerosis with tetraethylammonium chloride. **Neurology 2**:525 (Nov.-Dec.) 1952.

Williams, G. H., Jr., Nosik, W. A. and Hunter, J. A., Jr.: Convulsions as manifestation of multiple sclerosis. **J.A.M.A. 150**:990 (Nov. 8) 1952.

ERRATUM

On page 220, under the heading "ACTH and Cortisone," line 8 of the October 1952 *Quarterly* should read *Doctor Wijnbladh of Stockholm.*

THE FRANK E. BUNTS INSTITUTE

Announces the following Postgraduate Course for February 16-21, 1953

Given under the auspices of the American College of Physicians

A Postgraduate Course on "Pathology and Pathologic Physiology in Internal Medicine" will be given at the Clinic under the auspices of the American College of Physicians from February 16 through February 21, 1953. The course will place emphasis on pathologic anatomy and current concepts of pathologic physiology in systemic disease. The principal objective will be to stress the relationship between pathology, pathologic physiology, and clinical diagnosis and treatment. The major subjects to be presented will be in the field of cardiovascular and renal disease, pulmonary disease, gastroenterology, hematology, endocrinology, and metabolic diseases. The course will include lectures, clinical demonstrations, pathology conferences, and question and answer panels.

Tuition fees will be $30.00 for members of the American College of Physicians and $60.00 for nonmembers. Application should be made directly to Mr. E. R. Loveland, Executive Secretary, The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pennsylvania.

PATHOLOGY AND PATHOLOGIC PHYSIOLOGY IN INTERNAL MEDICINE

Tentative Program

Monday, February 16, 1953

8:00-8:50 a.m. . . Registration
8:50 a.m. . . . . Orientation . . . . A. C. ERNSTENE, M.D.

CARDIOVASCULAR DISEASE

9:00 a.m. . . . . Pathogenesis of Congestive Heart Failure . . . R. N. WESTCOTT, M.D.
9:30 a.m. . . . . The Mechanism of Edema . . . . C. J. WIGGERS, M.D. (Guest)
10:15 a.m. . . . . Cardiac Arrhythmias and Their Treatment . . D. C. HUMPHREY, M.D.
10:45 a.m. . . . . Intermission
11:00 a.m. . . . . Coronary Artery Disease . . . . A. C. ERNSTENE, M.D.
11:30 a.m. . . . . Treatment of Congestive Heart Failure . . . . W. L. PROUDFIT, M.D.
12:00 noon . . . Question and Answer Panel
12:30 p.m. . . . . Luncheon — Courtesy of the Bunts Institute

HYPERTENSION AND RENAL DISEASE

1:30 p.m. . . . . Pathogenesis of Essential Hypertension . . . . I. H. PAGE, M.D.
2:00 p.m. . . . . Renal Function Tests . . . . R. D. TAYLOR, M.D.
2:30 p.m. . . . . Fluid and Electrolyte Balance . . . . A. C. CORCORAN, M.D.
3:15 p.m. . . . . Intermission
3:30 p.m. . . . . Anuria and Uremia . . . . W. J. KOLFF, M.D.

4:00 p.m.	. . .	Pathology Conference: Renal Disease . . . . . J. B. HAZARD, M.D.,
		L. J. McCORMACK, M.D., A. C. CORCORAN, M.D., R. D. TAYLOR, M.D.
5:00 p.m.	. . .	Question and Answer Panel
6:30 p.m.	. . .	Reception and dinner for members of the Course and their wives at the Wade Park Manor.

Tuesday, February 17, 1953

ARTERIOSCLEROSIS, CARDIAC CATHETERIZATION, AND PULMONARY DISEASE

8:00 a.m.	. . .	Clinical Conference: Pathology and Pathologic Physiology of Peripheral Arterial Disease . . . . F. A. LeFEVRE, M.D., V. G. deWOLFE, M.D., J. B. HAZARD, M.D.
9:00 a.m.	. . .	Pathogenesis of Arteriosclerosis . . . . I. H. PAGE, M.D.
9:30 a.m.	. . .	Differential Diagnosis in Congenital Heart Disease . . . . F. M. SONES, JR., M.D.
10:15 a.m.	. . .	Intermission
10:30 a.m.	. . .	Mitral Commissurotomy: Pre- and Postoperative Studies . . . . F. M. SONES, JR., M.D.
10:50 a.m.	. . .	Pulmonary Function Tests and Pulmonary Emphysema . . . . R. N. WESTCOTT, M.D.
11:30 a.m.	. . .	The Pneumoconioses . . . . H. S. VAN ORDSTRAND, M.D.
12:00 noon	. .	Question and Answer Panel
12:30 p.m.	. . .	Luncheon — Courtesy of the Bunts Institute

GASTROINTESTINAL DISEASE

1:30 p.m.	. . .	Peptic Ulcer and its Complications . . . . . . E. N. COLLINS, M.D.
2:15 p.m.	. . .	Disorders of External Secretory Function of the Pancreas . . . . H. R. ROSSMILLER, M.D.
2:45 p.m.	. . .	Differential Diagnosis of Jaundice . . . . C. H. BROWN, M.D.
3:15 p.m.	. . .	Intermission
3:30 p.m.	. . .	Cirrhoses of the Liver and their Complications H. R. ROSSMILLER, M.D.
4:00 p.m.	. . .	Disturbances of Intestinal Absorption . . . . . C. H. BROWN, M.D.
4:30 p.m.	. . .	Question and Answer Panel

Wednesday, February 18, 1953

GASTROINTESTINAL DISEASE

8:00 a.m.	. . .	Pathology Conference: Diseases of the Liver . . J. B. HAZARD, M.D., L. J. McCORMACK, M.D., H. R. ROSSMILLER, M.D.
9:00 a.m.	. . .	Acute Intestinal Obstruction . . . . S. O. HOERR, M.D.
9:30 a.m.	. . .	Problems of Biliary Tract Surgery . . . . . . R. S. DINSMORE, M.D.
10:00 a.m.	. . .	Urologic Disease as a Cause of Gastrointestinal Symptoms . . . . W. J. ENGEL, M.D.
10:20 a.m.	. . .	The Irritable Colon . . . . E. N. COLLINS, M.D.
10:45 a.m.	. . .	Intermission
11:00 a.m.	. . .	Primary Amyloidosis . . . . R. A. VAN OMMEN, M.D.
11:30 a.m.	. . .	Systemic Lupus Erythematosus . . . . J. R. HASERICK, M.D.
12:00 noon	. .	Question and Answer Panel
12:30 p.m.	. . .	Luncheon — Courtesy of the Bunts Institute

1:30 p.m. . . .	Headache . . . . L. L. Lovshin, M.D.
2:15 p.m. . . .	Convulsive Disorders in Infancy and Childhood . R. D. Mercer, M.D.
2:45 p.m. . . .	The Muscular Dystrophies and Muscular Atrophies
	. . . . G. H. Williams, Jr., M.D.
3:15 p.m. . . .	Intermission
3:30 p.m. . . .	Reticulo-Endothelial Syndromes . . . . . . R. D. Mercer, M.D.
4:00 p.m. . . .	The Lipomatoses and Lipodystrophies . . . . . J. F. Whitman, M.D.
4:30 p.m. . . .	Question and Answer Panel

Thursday, February 19, 1953

HEMATOLOGY

8:00 a.m. . . .	Pathology Conference: The Leukemias and Malignant Lymphomas
	J. B. Hazard, M.D., L. J. McCormack, M.D., J. D. Battle, Jr., M.D.
9:00 a.m. . . .	Diagnostic Methods in the Classification of Anemias
	. . . . T. H. Ham, M.D. (Guest)
9:30 a.m. . . .	The Physiologic Mechanisms of the Hemolytic Anemias
	. . . . T. H. Ham, M.D. (Guest)
10:00 a.m. . . .	Sickle Cell Anemia and Mediterranian Anemia
	. . . . W. M. Fowler, M.D. (Guest)
10:45 a.m. . . .	Intermission
11:00 a.m. . . .	Polycythemia . . . . W. M. Fowler, M.D. (Guest)
11:30 a.m. . . .	Myeloid Metaplasia . . . . J. D. Battle, Jr., M.D.
12:00 noon . . .	Question and Answer Panel
12:30 p.m. . . .	Luncheon — Courtesy of the Bunts Institute
1:30 p.m. . . .	The Macrocytic Anemias . . . . . . W. M. Fowler, M.D. (Guest)
2:00 p.m. . . .	Hypochromic Anemia . . . . S. N. Goldhamer, M.D. (Guest)
2:30 p.m. . . .	Purpura and Hemophilia . . . . J. D. Battle, Jr., M.D.
3:00 p.m. . . .	Erythroblastosis . . . . Viola Startzman, M.D.
3:30 p.m. . . .	Intermission
3:45 p.m. . . .	Multiple Myeloma . . . . J. D. Battle, Jr., M.D.
4:05 p.m. . . .	Transfusion Reactions . . . . J. W. King, M.D.
4:30 p.m. . . .	Question and Answer Panel

Friday, February 20, 1953

ENDOCRINOLOGY AND METABOLIC DISEASES

8:00 a.m. . . .	Pathology Conference: Diseases of the Pancreas . J. B. Hazard, M.D.,
	L. J. McCormack, M.D., P. G. Skillern, M.D.
9:00 a.m. . . .	Principal Pathways of Intermediary Metabolism A. C. Corcoran, M.D.
9:30 a.m. . . .	Hypoglycemia . . . . P. G. Skillern, M.D.
10:00 a.m. . . .	The Role of Phosphatase . . . . J. R. Cook, M.D.
10:30 a.m. . . .	Intermission
10:45 a.m. . . .	Diabetic Acidosis and Coma, with Comments on the Use of
	Fructose in Therapy . . . . Max Miller, M.D. (Guest)
11:30 a.m. . . .	Hyperparathyroidism . . . . R. W. Schneider, M.D.
12:00 noon . . .	Question and Answer Panel
12:30 p.m. . . .	Luncheon — Courtesy of the Bunts Institute
1:30 p.m. . . .	Pathology of Diseases of the Thyroid Gland . George Crile, Jr., M.D.
2:00 p.m. . . .	Iodine Metabolism and the Action of Antithyroid Drugs
	. . . . J. R. Cook, M.D.
2:45 p.m. . . .	Hypothyroidism and Myxedema . . . . P. G. Skillern, M.D.

3:15 p.m. . . . . Intermission
3:30 p.m. . . . . Obesity and the General Principles of Fat Metabolism
. . . . R. W. Schneider, M.D.
4:00 p.m. . . . . Clinical Aspects of Disturbed Pituitary Function
. . . . E. P. McCullagh, M.D.
4:30 p.m. . . . . Question and Answer Panel

Saturday, February 21, 1953

ENDOCRINOLOGY AND METABOLIC DISEASES

8:00 a.m. . . . . Pathology Conference: The Adrenals, Ovaries, and Testes
J. B. Hazard, M.D., L. J. McCormack, M. D., E. P. McCullagh, M.D
9:00 a.m. . . . . Diagnosis and Treatment of Pheochromocytoma   A. L. Scherbel, M.D.
9:30 a.m. . . . . Addison's Disease . . . . E. P. McCullagh, M.D.
10:00 a.m. . . . . Adrenal Cortical Hyperfunction   . . . . . . R. W. Schneider, M.D.
10:45 a.m. . . . . Intermission
11:00 a.m. . . . . Therapeutic Effects of Estrogens and Androgens
. . . . E. P. McCullagh, M.D.
11:30 a.m. . . . . Question and Answer Panel. (A review of the Course)

Guest Speakers:

C. J. Wiggers, M.D. — Professor of Physiology, Western Reserve University School of Medicine, Cleveland, Ohio.

T. H. Ham, M.D. — Professor of Medicine, Western Reserve University School of Medicine, Cleveland, Ohio.

W. M. Fowler, M.D. — Professor of Medicine, State University of Iowa College of Medicine, Iowa City, Iowa.

S. N. Goldhamer, M.D. — Clinical Instructor in Medicine, Western Reserve University School of Medicine, Cleveland, Ohio.

Max Miller, M.D. — Assistant Professor of Medicine, Western Reserve University School of Medicine, Cleveland, Ohio.

THE FRANK E. BUNTS INSTITUTE

Announces the following Postgraduate Continuation Courses for
March 19 and 20, 1953.

MEDICAL AND SURGICAL DISORDERS OF THE URINARY TRACT

Tentative Program

Thursday, March 19, 1953

8:00-9:00 a.m. . . Registration
                    Morning Session . . . . C. C. Higgins, M.D., Presiding
9:00 a.m. . . . . Opening Remarks . . . . R. S. Dinsmore, M.D.
9:05 a.m. . . . . Clinical Significance of Hematuria . . . . . . C. C. Higgins, M.D.
9:25 a.m. . . . . Pyelonephritis and Glomerulonephritis . . . . . R. D. Taylor, M.D.
9:45 a.m. . . . Technic and Significance of Addis Count . . . . . H. P. Dustan, M.D.
10:05 a.m. . . . Diagnosis and Treatment of Carcinoma of the Prostate
               . . . . E. F. Poutasse, M.D.
10:25 a.m. . . . Intermission
10:35 a.m. . . . Diagnosis and Treatment of Hyperparathyroidism
               . . . . R. W. Schneider, M.D.
10:55 a.m. . . . Management of Patients with Renal Lithiasis . . C. C. Higgins, M.D.
11:15 a.m. . . . Management of Patients with Prostatism . . . . . W. J. Engel, M.D.
11:35 a.m. . . . Indications for and Management of the Artificial Kidney
               . . . . W. J. Kolff, M.D.
12:05 p.m. . . . Luncheon — Courtesy Bunts Institute
                    Afternoon Session . . . . W. J. Engel, M.D., Presiding
1:30 p.m. . . . Electrolyte and Chemical Features of Uremia . A. C. Corcoran, M.D.
1:50 p.m. . . . . Gastrointestinal Symptoms Associated with Urinary Tract Pathology
               . . . . C. H. Brown, M.D.
2:10 p.m. . . . Management of Surgical Patients with Cardiac Disease
               . . . . A. C. Ernstene, M.D.
2:30 p.m. . . . Diagnosis and Treatment of Nephrosis in Children
               . . . . Viola Startzman, M.D.
2:50 p.m. . . . Intermission
3:00 p.m. . . . Unilateral Renal Disease and Hypertension . . . . I. H. Page, M.D.
3:20 p.m. . . . Kidney Tumors — Clinical Aspects . . . . E. F. Poutasse, M.D.
3:40 p.m. . . . Kidney Tumors — Pathologic Aspects . . . . J. B. Hazard, M.D.
4:00 p.m. . . . Lower Nephron Nephrosis — Diagnosis and Treatment
               . . . . R. D. Taylor, M.D.
4:20-5:00 p.m. . Panel — Recurrent Urinary Tract Infections in Children
               . . . . C. C. Higgins, M.D. (Moderator)
                 R. D. Mercer, M.D., R. D. Taylor, M.D., W. J. Engel, M.D.
6:00 p.m. . . . Dinner — Courtesy Bunts Institute
8:15 p.m. . . . . Evening Lecture — Testicular Function   Warren Nelson, M.D. (Guest)

Friday, March 20, 1953

	Morning Session . . . . E. F. POUTASSE, M.D., Presiding	
9:00 a.m. . . .	Renal Lesions of Childhood . . . . R. D. MERCER, M.D.	
9:20 a.m. . . .	Treatment of Urinary Tract Infections . . . . . C. C. HIGGINS, M.D.	
9:40 a.m. . . .	Endocrine Problems of Interest to the General Practitioner
	. . . . E. P. McCULLAGH, M.D.	
10:00 a.m. . . .	Diagnosis and Management of Adrenal Tumors and
	Cushing's Syndrome . . . . E. F. POUTASSE, M.D.	
10:20 a.m. . . .	Intermission	
10:30 a.m. . . .	Bladder Neck Obstruction in Women and Children W. J. ENGEL, M.D.	
10:50 a.m. . . .	Translumbar Aortography:
	Diagnosis of Renal Lesions . . . . E. F. POUTASSE, M.D.	
	Diagnosis of Vascular Lesions . . . . A. W. HUMPHRIES, M.D.	
11:10 a.m. . . .	Diagnosis and Treatment of Congenital Anomalies of the
	Lower Urinary Tract . . . . C. C. HIGGINS, M.D.	
11:30 a.m. . . .	Diagnosis and Treatment of Tumors of the Bladder W. J. ENGEL, M.D.	
11:50 a.m. . . .	Electrocardiographic Aspects of Renal Failure . W. L. PROUDFIT, M.D.	
12:10 p.m. . . .	Luncheon — Courtesy Bunts Institute
	Afternoon Session . . . . C. C. HIGGINS, M.D., Presiding	
1:30 p.m. . . .	Recent Advances in the Treatment of Hypertension . I. H. PAGE, M.D.	
1:50 p.m. . . .	Psychic Factors in Urological Symptomatology . L. J. KARNOSH, M.D.	
2:10 p.m. . . .	Diagnosis and Treatment of Chronic Interstitial Cystitis
	. . . . E. F. POUTASSE, M.D.	
2:30 p.m. . . .	Diagnosis and Treatment of Congenital Anomalies of the
	Upper Urinary Tract . . . . W. J. ENGEL, M.D.	
2:50 p.m. . . .	Intermission	
3:00 p.m. . . .	Cardiac Arrest . . . . D. B. EFFLER, M.D.	
3:20 p.m. . . .	Diagnosis, Management, and Prevention of Anesthetic
	Complications . . . . D. E. HALE, M.D.	
3:50 p.m. . . .	Management of Surgical Patients with Diabetes
	. . . . E. P. McCULLAGH, M.D.	
4:10 p.m. . . .	Recent Developments in Hormone Production of Testes
	. . . . E. F. POUTASSE, M.D.	
4:20-5:00 p.m. . .	Panel — Surgical Injuries to the Urinary Tract in
	General Surgical Procedures . . . . W. J. ENGEL, M.D. (Moderator)	
	J. S. Krieger, M.D., R. B. Turnbull, Jr., M.D., C. C. Higgins, M.D.	

Guest Speaker:

Warren Nelson, M.D., Professor of Anatomy, University of Iowa.

REGISTRATION BLANK

Please register me for the course on "Medical and Surgical Disorders of the Urinary Tract" to be given March 19 and 20, 1953. (Registration Fee is $15.00, except for interns and residents, and members of the Armed Forces in uniform, who will be admitted free.)

I am enclosing check for $5.00 and the remainder will be paid on registration, March 19. Checks should be made payable to the Frank E. Bunts Institute.

Name ....

Address ....

Medical School and
Date of Graduation................................

This course is open only to graduates of approved medical schools.